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CRITICAL INTERPRETATION OF CLINICAL OBSERVATIONS

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Pearl [1] defines biometry as "that branch of science which studies by methods of exact measurement on the one hand, and precise and refined mathematical analysis on the other hand, the quantitative aspects of vital phenomena." There is certainly nothing new in a critical point of view in medical science, but too often it has led to nothing more than the negative result of skepticism. This is particularly true in clinical medicine, a growing percentage of whose practitioners are becoming conscious of the numerous modifying factors, often indeterminate, that influence living subjects. The essential attribute of living matter, as distinguished from so-called nonliving matter, consists in the relatively high variability of the former. One of the major divisions of the statistical method devotes itself to the measurement of variations, and no student of living matter should regard himself as properly equipped unless he has some knowledge of such technic. While it is a truism that chemistry and physics are exact sciences in that they deal with nonliving matter, nevertheless, as methods of measurement in these fields become more accurate and more sensitive, variability manifests itself more and more and makes the line of division between living and nonliving matter less and less distinct.

It has become axiomatic that medicine is an art as well as a science. Better, it might be stated that it is an art intelligently to apply scientific knowledge. There are still many procedures applied with the art which skill and experience bring but which can be reduced to the cold logic of figures. Contrary to the implication of the unfortunate and not even humorous story that there are liars, damned liars and statistics, figures do not lie—although, it is true, they may be made to deceive in the hands of those who do not know how to use them. It it quite true, as Pearl [2] states, that "it is not to be expected, or perhaps even desired, that every medical practitioner or investigator shall be an accomplished mathematician." Nevertheless, in the analysis of his observations and the presentation of his results, the author should use the proper methods that are available. Many earnest workers who would scorn to use laboratory methods or instruments that have been long out of date still employ methods of analysis that render doubtful their conclusions or may even falsify them. The intelligent reader, too, must be aware of the terminology of statistical science and learn to think in its terms. One who would do nothing more than read the lucid first chapter of Pearl's book will at least gain an understanding of what the mathematician has to offer to clinical medicine. The judgment of the physician, which so largely determines the difference between doctors and good doctors, must always be a factor, since statistical analysis is concerned with groups and not individuals. All this does not countenance the continuation of incorrect procedures or uncertainty, or the passing on from one generation to another of impressions which are susceptible of proof or of denial.

It is obvious that the time at disposal allows only a plea for more general application of statistical methods in medicine, and the illustration of a few of the simplest examples of what it accomplishes.

REQUISITES OF STUDY

The first requisite of any study is an unbiased survey of the accuracy of the observations. One must see with a clear eye, palpate with a sensitive hand, listen with a sharp ear and note with an unprejudiced brain—avoiding by all means forcing the senses to interpret as the preformed conception dictates. It is easier, furthermore, to make rigid and pure one's own method of observation than to control the mental processes of others, and, in studies in which several investigators are involved, special attention must be directed at the so-called personal equation. The difficulties mentioned have led certain biometrists to discount many clinical observations. For example, I have heard it maintained that no physician can tell when a child is suffering from malnutrition. This is a silly assertion if meant literally. One does not need mathematical proof that malnutrition exists when it is marked, any more than one requires a thermometer to tell that water is hot when it burns one's skin. In borderline cases, however, the need for accurate analysis of clinical data is greatest.

One of the commonest errors of the unwary is the assumption that certain types of observation are worthy of record. Obviously it is futile and misleading to subject to critical study data that may be false. The point can be illustrated by referring to a subject that has often been mistreated; namely, the benefits derived from tonsillectomy.[3] In many conditions the results of tonsillectomy are disappointing. Part, at least, of the unfulfilled expectations is due to the acceptance of unreliable statements from honest but mistaken sources, and to the failure to take modifying factors into

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Read before the Section on Pediatrics at the Eighty-Sixth Annual Session of the American Medical Association, Atlantic City, N. J., June 12, 1935.

1. Pearl, Raymond: Introduction to Medical Biometry and Statistics, ed. 2, Philadelphia, W. B. Saunders Company, 1918, p. 18.
2. Pearl: Introduction to Medical Biometry and Statistics, p. 21.
3. Selkirk, T. K., and Mitchell, A. G.: Evaluation of the Results of Tonsillectomy and Adenoidotomy, Am. J. Dis. Child. **42**: 9 (July) 1931.

consideration. Thus, while positive statements are frequently made concerning the beneficial effect of tonsillectomy on respiratory infections, it is not easy to prove that this association is direct cause and effect. To accept this as *post hoc ergo propter hoc* fails to take into account such factors as the individual's inherent resistance, acquired immunity, exposure, other diseases of the respiratory tract, season, age, sex, hygienic conditions and the like. Furthermore, how reliable is the casual statement of the mother or patient concerning the frequency and severity of respiratory infections over a period of years? How many physicians, without having made it a matter of special record, would be able accurately to state their own medical histories in such detail? Why, then, accept such statements on their face value from parents who obviously cannot give them accurately and who may be influenced by faith in the doctor or lack of it? How often, too, has the known influence of age on the incidence of rheumatic diseases been neglected in studies on the after-effect of tonsillectomy? One could cite such examples indefinitely. Parenthetically, it should be stated that no attempt has been made here to prove that tonsillectomy is without value, and the subject has been employed merely as a familiar illustration.

TABLE 1.—*Depression of the Skin Response During the Acute Stage of Diseases in Persons Normally Giving Positive Reactions to Tuberculin*

		Positive Reaction to Tuberculin Test				
		Febrile Stage		Convalescent Stage		
Disease	Number of Cases	Number	Rate	Number	Rate	$\frac{K}{PE_K}$
Scarlet fever....	854	35	0.041 ± 0.007	179	0.210 ± 0.014	10.88
Measles.....	283	19	0.067 ± 0.015	50	0.177 ± 0.023	4.04
Diphtheria.....	140	16	0.114 ± 0.027	27	0.192 ± 0.033	1.83
Miscellaneous...	210	12	0.057 ± 0.016†	23	0.110 ± 0.022	....
Poliomyelitis.	38	3		3		
Varicella.....	57	4		12		
Pertussis.....	79	3		3		
Mumps.....	4	0		0		
Other diseases	32	2		5		
Total.....	1,487	82	0.055 ± 0.006	279	0.188 ± 0.010	11.29

There must be mentioned the subject of "control." It is, in fact, the thoughtless assumption that a study has been properly controlled that has led to so many errors. Workers in the laboratory are often faced with considerable uncertainty in regard to the adequacy of their controls, especially when living material is involved. How much more skeptical should the investigator be when he is dealing with human material, in which endogenous and exogenous factors, often indeterminable, are legion.

STATISTICAL ANALYSIS

Having reasonable assurance that the data to be studied are acceptable, what shall be done with them? Sometimes their meaning is more or less obvious, at others quite obscure. Under the latter conditions one can turn to the devices of the statistician, many of which are available to the ordinary intelligence. That is to say, a person need not be accomplished in advanced and intricate mathematics to become helpfully proficient in the use of certain formulas. He need not necessarily have knowledge of the genesis or derivation of these devices but may accept and employ them on faith, much as he does laboratory instruments the manufacture and standardization of which he is willing to delegate to others. I can best illustrate by a few examples from actual experience with statistical analysis of clinical problems and a demonstration of some of these mathematical devices.

In our studies of the influence of various conditions on specific skin reactions, my associates and I have noted the effect of several diseases on the skin reaction to tuberculin. It has been frequently stated that measles might cause the tuberculin reaction to become negative. The results of our own observations [4] in measles and other diseases may be recorded as in table 1. The mathematical criterion employed in the analysis is that if the use of the formula $\frac{K}{PE_K}$ gives a result greater than 4 the result is significant, but that if it is less than 4 it is not significant. In this particular case, K equals the difference between the rates [5] of occurrence of positive reactions in the febrile and convalescent stages, and PE_K equals the probable error of this difference. It can be seen from the table that it is fair to state that scarlet fever has a greater effect on the tuberculin reaction than measles, since the figure 10.88, derived from the use of the formula $\frac{K}{PE_K}$, indicates, according to mathematical calculation [6] that the chances are about 70 billion to 1 that the difference between the rate of the skin reaction to tuberculin in the acute and convalescent stages is not due to chance, whereas in measles the figure 4.04, while still probably significant, indicates a mathematical probability of only about 140 to 1 that the difference is not due to chance alone. Such a concept certainly conveys a much more accurate idea of the existing situation than does a simple percentage difference.

A further advantage of statistical analysis is the ability to indicate the amount of material necessary to elicit significant results. For example, the figure 1.83 (table 1) is the difference between the rates of the tuberculin reaction in the acute and convalescent stages of diphtheria divided by the probable error of that difference. This cannot be accepted as significant, since such a difference would arise by chance alone approximately twenty-five times out of 100 without the operation of any causal factor—this not being regarded as statistically acceptable proof that it might not be a chance phenomenon. However, the rates of reaction in both the acute and the convalescent stage of diphtheria are stable; i. e., in any given number of cases, tests made in the same way under the same conditions should give approximately the same rate. In other words, from a statistical point of view it is not necessary to study this further, since multiplication of cases would not change the result. A better illustration of the value of the statistical method in this respect is obtained in our observations on the effect of scarlet fever on the tuberculin reaction. Several years ago we [7] studied the tuberculin reaction during the acute and convalescent stages in 435 cases of this disease and

4. Mitchell, A. G.; Nelson, W. E., and LeBlanc, T. J.: Studies in Immunity, Am. J. Dis. Child. **39**:696 (March) 1935.

5. The term rate as used in biometry indicates the number of times a specific kind of event actually occurs divided by the times it might occur in the "universe" under consideration. In this instance, for example, the rate of positive tuberculin reactions during the acute stage of scarlet fever was $\frac{35}{854} = 0.041$. To determine that a rate is stable it must, when divided by its probable error, give a figure greater than 4. In this instance the PE (probable error) was found to be ±0.007, so that 0.041 divided by 0.007 was 5.86, a significant figure, which indicates that the rate was stable.

6. Pearl: Introduction to Medical Biometry and Statistics, p. 438, appendix III, table A.

7. Eddy, Bernice, and Mitchell, A. G.: Studies in Immunity, Am. J. Dis. Child. **40**:771 (Oct.) 1930.

found that 4 per cent of the patients had a positive reaction during the acute stage, whereas 19 per cent had a positive reaction during convalescence. If we had then applied statistical methods instead of amassing more figures, we would have found that the rates of the tuberculin reaction were stable during both the acute and the convalescent stage and that the rate was significantly higher in the convalescent stage. That is to say, the probability that the difference was not due to chance alone was about 500 million to 1. This is sufficient evidence that further study of this fact was hardly necessary, since the conventionally acceptable threshold is placed at odds of about 1,000 to 1.

The illustrations already given argue for the fact that the statistical treatment of data almost invariably leads to a clearer statement of the problem and cleaner and sharper attack on it. Too often, in clinical medicine, research consists of collecting a large amount of data and then attempting to find out what the data reveal—or conceal. The statistical technic would tend to reverse this process by first setting up the question and then indicating what data were essential to a final answer. It is of more than passing interest that the literature contains many papers demonstrating much labor in securing and gathering data from which incorrect conclusions have been drawn or in which the method of analysis is questionable. This section is not guiltless in its presentations, some of which have led to argument and discussion when statistical study would have obviated uncertainty.

The question is often asked "How many cases must be studied to answer a certain question?" A better way of stating this is "What should be the size of the sample from the 'universe'?" Investigators are almost always concerned with differences between experimental and control, and since studies on living material must of necessity be conducted on samples and never on an entire universe, there is always present the question of the sampling error or of variations arising because of the size of the sample. This is really an application of the probable error concept. The size of the sample depends on the question to be answered and the variability of the observations considered. It is evident that much work continues on matters that had previously been solved. Our own interest in the effect of scarlet fever antitoxin may illustrate this.[8] For example, by observation of the effect of the administration of scarlet fever antitoxin on the incidence of complications in 112 patients and using as a control group in the same epidemic eighty-four patients, it was found that in the antitoxin-treated patients sixteen complications (14.6 per cent) developed, whereas forty-seven complications (56.1 per cent) developed in the patients who were not given antitoxin. Analyzing statistically by means of the chi-square test (which is a special application of the theory of probability) there remains no doubt of the significance of this difference in the two groups, since the figure 39.2 is obtained for chi square which indicates that the probability that the difference was not due to chance alone is over 500 million to 1. In the paper presented before this section last year by Lucchesi and Bowman [9] figures were given on 3,045 patients treated by antitoxin and 2,332 patients who did not receive antitoxin. In the first group complications developed in 18.8 per cent, and in the second group in 26.2 per cent. These figures suggest a difference in favor of the antitoxin-treated group but do not leave a flavor of finality. If the chi-square test had been applied, it could have been demonstrated that the probability that the difference was not due to chance alone was over 400 billion to 1 (chi square = 78.4). That is to say, the 196 cases that we had studied constituted a sufficient number to arrive at practically the same conclusions as the 5,377 cases of Lucchesi and Bowman. It may be stated, however, that the large number of cases presented by these workers demonstrated that it was only adenitis that could be proved to be influenced by antitoxin, and that our own series of cases was too small to permit study of the influence of antitoxin on individual complications. Any analysis such as has just been given, of course, does not consider such factors as severity, type of epidemic or age.

Statistical analysis can frequently decide on the value of clinical procedures and lead to the adoption of satisfactory technic. For example, in connection with studies on anemia in the Children's Hospital discussion arose concerning the relative accuracy of five different methods of counting erythrocytes. Only one factor—namely, dilution—need be discussed by way of illustration. If three different dilutions are made, 1:100, 1:200 and 1:500, of the same sample of heparin blood (other factors, as the type of pipet and counting chamber, the time and degree of shaking remaining the same) and the mean, the probable error and the coefficient of variability calculated for each dilution, it is found that, while the means are almost invariably within the limit of error, the probable error and the coefficient of variability increase very materially with dilution (table 2). Since this happens consistently with a large number of samples, even when different technicians perform the counts and provided the total count is not excessively high, the conclusion is clear that a dilution of 1:100 is more accurate from the standpoint of being subject to substantially less variability than a dilution of 1:200 or 1:500.

TABLE 2.—*Increase of Probable Error and Coefficient of Variability with Dilution*

Dilution	Mean Red Blood Cells, Million	Probable Error, Million	Coefficient of Variability, per Cent
1:100	3.439	±0.033	± 0.10
1:200	3.495	±0.040	±10.60
1:500	3.500	±0.074	±19.60

Time will not permit a discussion of several other frequently applicable statistical devices as correlation, the histogram, the polygon and curve fitting.

SUMMARY

The fact that clinical observations should be applied in the diagnosis and treatment of human ailments makes it essential that they shall be interpreted as correctly as possible. Statistical analysis should be employed to a much greater extent in clinical and laboratory investigation than is the case at present. The first requisite of any study is the assurance that the material to be analyzed is acceptable and that the control is really comparable. The operation of the law of chance can often be stated with precision rather than in the uncertainty of percentage comparison. Needless work and waste of time and material may often be avoided by statistical analysis. It should be emphasized that mathematical treatment relates in general to group

8. Veldee, M. V.; Stevenson, F. E., and Mitchell, A. G.: Pub. Health Rep. **46**: 3023 (Dec. 18) 1931.
9. Lucchesi, P. F., and Bowman, J. E.: Antitoxin versus No Antitoxin in Scarlet Fever, J. A. M. A. **103**: 1049 (Oct. 6) 1934.

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reactions and not to individual instances with which the clinician may be dealing and which may not follow the average but manifest peculiarities or represent extremes in the group. Statistical analysis does not obviate the necessity for thought and judgment.

Children's Hospital.

THE SIMULATION OF INTRACRANIAL TUMOR BY LEAD ENCEPHALOPATHY IN CHILDREN

WITH REMARKS CONCERNING THE SURGICAL TREATMENT OF THE LATTER

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Lead encephalopathy may present all the signs and symptoms of intracranial tumors in children. A group originally thought to be cases of intracranial neoplasm, but subsequently classified as examples of "serous arachnoiditis" because of the absence of any signs of tumor at operation, have recently been shown to be examples of intoxication with lead.

CASE 1.—*Roy C., aged 2 years; vomiting three months; two convulsions; staggering gait; large head; "cracked pot" sound; choked disks; hypo-active reflexes; glycosuria; separated cranial sutures; suboccipital decompression, no tumor found; demonstration of lead poisoning, lead line in roentgenograms, lead in blood, urine and feces; no anemia, lead line on gums or stippling of erythrocytes; complete recovery.*

The patient who first drew our attention to the possibility that some of our cases of "pseudotumor" or "serous arachnoiditis" were really examples of lead encephalopathy was a small boy (Roy C.), aged 2 years, who was referred to us by Dr. Joseph Brennemann of the Children's Memorial Hospital, Chicago.

History.—Roy was admitted to the Bobs Roberts Hospital of the University of Chicago Clinics, Oct. 6, 1934. His parents stated that he had been a healthy child except for mumps at about 5 months of age, and a fall from his bed at 1 year, until three months prior to his admission. At that time he and his twin brother developed a diarrhea following the ingestion of some loose plaster from the kitchen wall. The twin was given castor oil, which he retained, and he soon recovered. The patient vomited the castor oil and also food taken that day. Subsequently he suffered from bouts of vomiting of increasing frequency. Six weeks prior to admission the patient had a convulsion, apparently tonic in character, which lasted about two minutes. Two days prior to admission he had a clonic convulsion which lasted for one and one-half hours. The parents had also observed that the child had become restless and irritable and that he frequently sucked his fingers. For a few days prior to admission the child seemed uncertain in walking and had fallen on several occasions.

Examination.—Physical examination revealed that the child was well nourished. His head was large for his age and the superficial veins of the scalp were dilated. Percussion of the head, which distressed the child greatly, elicited a typical cracked pot sound (Macewen's sign). The child did not speak or seem to comprehend simple commands. He was able to walk, but only with his feet spread wide apart. However, he did not stagger or fall. On sitting up the patient had difficulty in maintaining his balance.

There was a definite choking of both optic disks of from 2 to 2.5 diopters. No hemorrhages or exudates were seen in either fundus oculi. The pupils were round, equal and reacted rather slowly to light. Ocular movements were full in all directions, and there was no nystagmus. There was no other evidence of any involvement of the cranial nerves. No sensory loss could be detected. All extremities were abnormally flaccid but no localized weakness was present. All deep tendon reflexes were hypo-active. Babinski's sign was not present.

Urinalysis repeatedly revealed large quantities of a reducing substance in the urine. An examination of the blood (nonfasting) revealed 138 mg. of dextrose per hundred cubic centimeters. A dextrose tolerance test was reported as normal. A blood count showed 13,800 white blood cells, 65 per cent polymorphonuclear leukocytes, 4,800,000 erythrocytes and 70 per cent hemoglobin.

Roentgenograms of the skull revealed definite, though moderate separation of all the cranial sutures (fig. 1).

A diagnosis of a midline tumor of the posterior cranial fossa was made, either a medulloblastoma of the vermis or an ependymoma of the fourth ventricle being suspected.

Operation.—A suboccipital craniectomy was performed, October 11. Puncture of the left lateral ventricle through the occipital lobe revealed a dilated ventricular system containing clear colorless cerebrospinal fluid under considerably increased pressure. Both the cerebellum and the fourth ventricle, which were thoroughly exposed, appeared entirely normal. At the close of the operation a flanged needle was left in the left lateral ventricle in order to prevent a postoperative rise in intracranial pressure.

Postoperatively a diagnosis of "serous arachnoiditis," similar to that seen in the case of Esther S. (case 2), who had been operated on in 1931, was made.

Following the operation the patient's condition was very satisfactory. The ventricular needle drained profusely until removed two days after operation.

Demonstration of Lead Poisoning.—Shortly following the operation it was suggested by Drs. E. S. James and D. Pachman of the pediatric resident staff that the patient might be suffering from lead poisoning. Immediate and repeated examinations failed to reveal any lead line on the gums or basophilic stippling of the red blood cells. Cerebrospinal fluid was repeatedly collected until 62 cc. had been obtained. This contained 0.025 mg. of lead. In 703 cc. of urine 0.100 mg. of lead was found, and 106 Gm. (wet weight) of feces contained 0.025 mg. of lead. Blood drawn on October 24, and again on November 27, was submitted to Dr. Harold Blumberg of Johns Hopkins Hospital, who examined it spectrographically and reported 0.2 mg. of lead per hundred cubic centimeters of blood in the first sample, which he stated "would indicate clinical lead poisoning or an early stage of convalescence from it," and 0.1 mg. per hundred cubic centimeters in the second sample, which he considered evidence of "mild clinical or subclinical lead poisoning." In addition, Dr. Blumberg's examination revealed a slight argyremia, and subsequent inquiry revealed that the mother had frequently dropped mild silver protein in the patient's nose. Roentgenograms were made of the various long bones, and these revealed marked bands of increased density at the ends of the diaphyses (fig. 2).

Subsequent Course.—The patient's condition rapidly improved. The choked disks soon subsided, fortunately without any optic atrophy. The cerebrospinal fluid pressure soon returned to normal.

Under the direction of Dr. Bengt Hamilton of the department of pediatrics, the child was given phosphorized cod liver oil in order to facilitate the removal of lead from active circulation and hasten its storage in the bones.[2] Under this treatment the dense bands at the ends of the bones rapidly widened (fig. 2). This increase in the density of the bands at the ends of the long bones may indicate increased calcium deposition as a result of the administration of phosphorized cod liver oil, the continued storage of lead or both.

The child was discharged, November 29, completely recovered from the lead encephalopathy.

From the Division of Neurology and Neurosurgery of the University of Chicago Clinics.

Owing to lack of space, this article has been abbreviated for publication in THE JOURNAL. The complete article appears in the authors' reprints.

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2. The utilization of phosphorized cod liver oil for this purpose is being experimentally investigated and will be the subject of a later report by Dr. Hamilton.

Family History.—The family consisted of the mother (J. C., aged 30), the father (Ralph C., aged 34) and three brothers (Gilbert, aged 6, Wallace, aged 3½, and Ray, the twin brother of the patient). The father's history was not significant. The mother had suffered from convulsions in infancy but had had no major illnesses since. All the children had had abnormal appetites and eaten many strange things, including paint from the wall, furniture, toys, and the like. Roy, the patient, had been the greatest offender in this regard and while in the hospital had amply demonstrated this perverted appetite

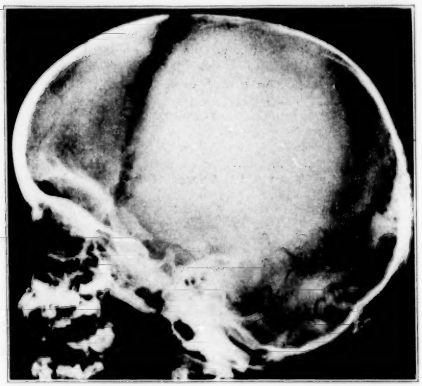

Fig. 1 (case 1).—Appearance of the skull, Oct. 8, 1934. The coronal and parieto-occipital sutures are all markedly separated.

by chewing the tables and the arms of the chairs. Except for ingestion of plaster, the history of the twin brother Ray is not significant. Both Gilbert and Wallace had each had three convulsions and each such attack was associated with vomiting. These, however, had occurred months or years prior to Roy's illness. Roentgenograms of the wrists of the three brothers revealed nothing abnormal, so that these convulsions could not be definitely associated with lead intoxication.

Samples of the paint and plaster from the kitchen wall were shown to contain large quantities of lead.

There would seem to be little question as to the diagnosis of lead encephalopathy in this case. The history of the eating of plaster prior to the onset of the symptoms that led to the child's admission to the hospital was unwisely disregarded in making the diagnosis of cerebellar tumor. This history should have suggested the possibility of lead encephalopathy.

The occurrence of similar clinical pictures in cases of lead poisoning in children has been reported by McKhann [3] and other observers. The absence of a lead line on the gums, anemia and stippling of the red blood cells in this case is not surprising, as their absence has been noted by others in cases of proved lead poisoning in children. The definite line of increased density at the ends of the bones in a child that had had no previous phosphorus administered, no viosterol and had apparently not suffered from rickets is very suggestive if not conclusive evidence of lead poisoning, while Dr. Blumberg's demonstration of lead in the blood is definite proof. The absence of any considerable amount of lead in the urine or feces is readily explained by the fact that the child had been removed from his source of lead for a considerable period of time prior to the examination of the excreta.

3. McKhann, C. F.: Lead Poisoning in Children: The Cerebral Manifestations, Arch. Neurol. & Psychiat. **27**: 294-304 (Feb.) 1932.

That the convulsions from which the mother and two older boys suffered in infancy were due to lead intoxication cannot be proved, but the two boys were known to be afflicted with perverted appetites and there exists the possibility that the metal may have played some part in their cases. Ray, the twin, was probably saved from more severe lead poisoning by the catharsis with castor oil, as well as by the less marked pica which he showed in comparison with his brother Roy.

It will be recalled that at the time of operation we were impressed by the similarity between this case and other cases in this clinic which have been diagnosed as "serous arachnoiditis," particularly the case of Esther S. The histories and available roentgenograms of all such cases were reviewed and new roentgenograms of the long bones were made of all patients that could be located. In only one case, that of Esther S., were we able to establish a presumptive diagnosis of lead intoxication. Too long a period of time had elapsed in all cases to anticipate the demonstration of lead in the blood or excreta in any of these old cases and thus to establish a positive diagnosis. That it was impossible to establish the diagnosis of lead intoxication in the other cases of "serous arachnoiditis," which were mostly in

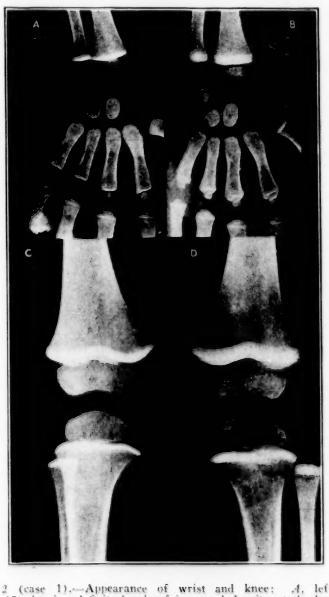

Fig. 2 (case 1).—Appearance of wrist and knee: *A*, left wrist, October 17, showing definite bands of increased density at the lower ends of the radius and ulna and to a less extent at the peripheral ends of the phalanges; *B*, the same wrist two months later (December 10), after daily administration of phosphorized cod liver oil. The bands are more than twice as wide. *C*, "lead lines" at the ends of the femur, tibia and fibula before the institution of therapy directed toward the storage of lead, October 19; and *D*, the same bones two months later, December 10.

children, does not completely exclude that possibility, as the reinvestigation was carried out several years after the acute episodes. The establishment of the proper diagnosis in the case of Esther S. was largely dependent on fortuitous circumstances.

CASE 2.—*Esther S., aged 5 years; vomiting, constipation and headache three weeks; crossed eyes one week and stiffness of the neck; large head; "cracked pot" sound; choked disks of 4 diopters; bilateral external rectus palsies; flaccidity of extremities; reduced reflexes; positive Babinski; incoordination; walked on a wide base; normal blood and urine; separation of cranial sutures; diagnosis, midline cerebellar tumor; no tumor found at operation; "serous arachnoiditis"? complete recovery; subsequent demonstration of "lead line" in long bones in original and later roentgenograms; elicitation of history of pica.*

History.—Esther S., aged 5 years, referred to the University of Chicago Clinics by Dr. Joseph Brennemann, was admitted, July 17, 1931. Her parents stated that she had been perfectly well until three weeks before admission, at which time she began to vomit, at first only once or twice a day. The vomiting became progressively more severe and frequent, until during the ten to fourteen days before admission she had been almost unable to retain any food or fluids. The vomiting was not associated with nausea and the child complained of hunger. At about the same time the bowels became severely constipated and evacuation by any means was very difficult.

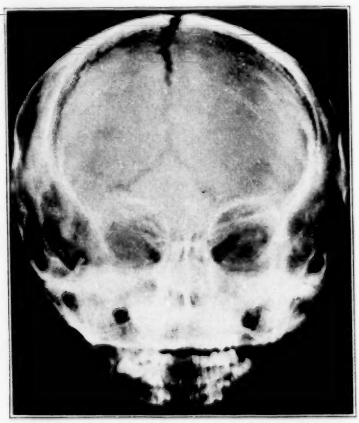

Fig. 3 (case 2).—Appearance of the skull, July 18, 1931. The sagittal and parieto-occipital sutures are definitely separated. Some "digital" markings are visible, especially on the right.

With the onset of the vomiting the patient began to complain of headache, which was present daily, was variable in severity and was not localized. One week before admission she began to complain of impaired vision and said "everything looks funny." About that time her mother noted that her eyes were crossed, the left being turned in. Four days before admission, stiffness of the back of the neck developed.

Her birth, dietary and developmental histories were not abnormal. She had suffered from measles at 17 months and scarlet fever at 2 years, following which she had had an infection with discharge from the right ear.

Examination.—General physical examination revealed nothing abnormal. On neurologic examination it was found that the head was enlarged and gave a "cracked pot" sound on percussion. The optic disks presented a choking of 4 diopters. There were many small hemorrhages over the disks, a few in the retina and some patches of white exudate. It was impossible to test the visual acuity or visual fields because of the lack of cooperation. The pupils were round and equal and reacted normally. There was a bilateral weakness of the external recti, greater on the left. There was definite flaccidity of all four extremities and distinct incoordination on the finger-to-nose test on the left. The tendon reflexes were hypo-active, the right knee jerk being more reduced than the left. At times a bilateral Babinski sign could be elicited. The child walked with her feet spread wide apart and with a staggering gait.

Laboratory Examination.—Urinalysis revealed no abnormality. The blood examination showed 7,800 white blood cells, 4,700,000 red blood cells and 85 per cent hemoglobin. The blood Wassermann and Kahn tests were negative, as were the intradermal tuberculin tests. Roentgenograms of the skull were reported as showing only separation of the cranial sutures and digital impressions on the inner table of the skull (fig. 3).

A diagnosis of a midline cerebellar tumor (probably a medulloblastoma) was made.

Operation.—July 23, the patient was operated on by the usual suboccipital approach. Puncture of the left lateral ventricle revealed a grossly dilated ventricular system containing clear colorless fluid under moderately increased pressure. The cerebellum, meninges, cisterna magna and fourth ventricle appeared normal. The vermis was incised in the midline but no tumor was found. The unsatisfactory diagnosis was made of "acute internal hydrocephalus of unknown origin."

The patient made a rapid and uneventful postoperative recovery. Following her discharge from the hospital the patient soon returned to normal activity. There is at present no detectable evidence of any neurologic or mental impairment.

Discovery of Lead Poisoning.—After our experience in case 1, Esther was asked to return to the hospital for roentgenograms of the long bones. The right knee and wrist were roentgenographed, Oct. 26, 1934 (fig. 4). The ends of the long bones, as was to be expected, were perfectly normal, but in the shaft of the long bones there was a line of increased density, about 1 mm. in width. This line was 3.7 cm. above the lower epiphyseal line in the femur, 2.1 cm. below the epiphyseal line in the tibia and 1.9 cm. above the epiphyseal line in the radius. The old films of the skull were then reviewed. Fortunately in one corner of some of the films the head and upper end of the humerus was visible. At the upper end of the diaphysis could be seen a very definite wide line of increased density, typical of "lead lines" occurring in this location.

In addition, inquiry elicited from the parents a definite history of pica in this case, although no specific instance of the ingestion of lead or lead-containing substances could be recalled.

Although the diagnosis of acute lead encephalopathy can never be positively established in this case, many things point to that as the correct interpretation.

The history of the sudden onset of vomiting, constipation, headache, strabismus and stiffness of the neck, with the finding of definite evidence of severely increased intracranial pressure and of no tumor at operation, the demonstration of lines of increased density in the metaphyses of the bones at the time of the acute illness and of similar lines at a considerable distance from the ends of the long bones after more than three years of growth and the elicitation of the definite history of pica preceding the acute illness make the diagnosis of acute lead encephalopathy as nearly certain as is possible after the elapsing of this period of time.

Both of the preceding cases are also of great interest because of the rapid and apparently complete recovery following the making of a decompression.

The third case presented a much less difficult diagnostic problem but is included, as it is the only other case of acute lead encephalopathy with sufficiently increased intracranial pressure to simulate a tumor that has been seen and recognized in the University of Chicago Clinics. As the case was never seen by either of us, the record will be only briefly presented:

CASE 3.—*Girl, aged 6½ years; admitted Oct. 15, 1930; attacks of epigastric pain for years; one attack of jaundice and vomiting; difficulty in walking; bilateral foot drop; absent ankle jerks; slight blurring of optic disks; anemia; stippled*

erythrocytes; diagnosis acute anterior poliomyelitis? or peripheral neuritis (lead)? Discharged October 27.

Readmitted November 11; bilateral papilledema; right facial weakness; internal strabismus; separation of the cranial sutures; normal ventriculogram; large amount of lead in feces; "lead lines" ? in the bones; viosterol and calcium therapy; slow recovery.

History.—Betty, J. E., aged 6½ years, admitted to the University of Chicago Clinics, Oct. 15, 1930, had for several years suffered from attacks of epigastric pain and severe anorexia. In the spring of 1928 she had been jaundiced and had vomited repeatedly. In August 1930, during an attack of whooping cough, she had vomited often and had no appetite. In September, difficulty in walking and slight aching pains in the thighs developed for which she was admitted to the hospital.

Examination.—Physical examination in October 1930 revealed pallor, a systolic apical cardiac murmur and a distended bladder, which was readily evacuated. She had a bilateral foot drop and was unable to move her toes. The quadriceps extensors were also weak. The ankle jerks were absent. The right optic disk was slightly blurred.

The blood count revealed an anemia of 3,510,000 red blood cells, and smears showed marked basophilic stippling.

Discharge.—The child was discharged, October 27. There was a difference of opinion as to whether the correct diagnosis was peripheral neuritis due to lead poisoning or acute anterior poliomyelitis.

Readmission.—November 11 there was a bilateral papilledema of from 2 to 2.5 diopters, and the child was readmitted to the hospital.

Further inquiry elicited the fact that in April 1930 the patient had eaten an unknown quantity of white house paint.

Reexamination on November 11 and 15 revealed the foot drop and reflexes as before, a papilledema, a right facial weakness and a right external rectus paralysis. No lead line along the gums could be found. The blood showed an anemia and stippled red cells, which rapidly decreased in number, and none were found December 19.

Demonstration of Lead.—December 6, Dr. C. W. Muehlberger, who had kindly examined the excreta, reported that 224 Gm. of feces collected between November 13 and 16 contained 22.6 mg. of lead.

Roentgenograms of the skull, taken November 13, revealed slight separation of the sutures and increased digital or "convolutional" markings on the inner table of the skull (fig. 5). A ventriculogram was made, November 17. The intracranial tension was greatly increased but the ventricular system was normal (fig. 5). Roentgenograms had been taken of various parts of the body on October 17 and 22 and November 13, 17 and 29 and, except for those of the skull, were reported as normal. December 16, additional roentgenograms of the long bones were made. On reviewing the earlier films slight lines of increased density at the ends of the metaphyses were made out, whereas those last taken showed definite and wider lines (fig. 6). However, as large doses of viosterol and calcium lactate had been administered in the interval, the lines were not considered very significant.

Course.—Following the ventriculogram the child was stuporous and later lethargic for more than two weeks and the papilledema was considerably increased. December 2 the choked disks were receding, but there was a bilateral external rectus paralysis, complete on the right and partial on the left. Conjugate movement of the eyes upward was impossible. There was a right facial weakness. The foot drop was still present, but the ataxic gait was considered to be much more severe than it would explain. Slowly her condition improved and she was discharged, Jan. 9, 1931. The external rectus palsy had practically subsided. The optic disks and vision were normal. The foot drop was unchanged. She was last seen, May 6. The foot drop was much better and her general condition was said to be good. Unfortunately, there is no statement as to her mental condition. Since then all track of her has been lost.

This child differs primarily from the others in that the initial symptoms were those of a peripheral neuritis. Not until several weeks later did signs of increased intracranial pressure develop, and this was much less severe than in the other two cases, in which headache and vomiting were pronounced symptoms and the lateral ventricles were grossly dilated. At no time was there any evidence of any localized intracranial lesion. The history of the ingestion of lead and the finding of a peripheral neuritis purely motor in type, an anemia, stippled red blood cells, and a large quantity of lead in the feces would seem to make the diagnosis of lead intoxication certain. In this particular case the roentgenograms of the long bones were of little or no diagnostic value.

Although there is no information concerning the child's present condition, her recovery would appear to be an unusually fortunate and exceptional one, particularly in that she recovered from a severe papilledema without developing an optic atrophy. In view of the rapid recovery in cases 1 and 2 as compared with the very slow recovery in this case, it would appear likely that this child would have been saved a long and severe illness by a decompression.

Fig. 4 (case 2).—*A*, portion of shoulder unintentionally included on the film of the skull taken on July 18, 1931. A line of increased density is plainly visible at the upper end of the humerus. *B*, same shoulder also included in a roentgenogram of the skull taken Jan. 11, 1932, six months after *A*. The line of increased density is now a short distance from the epiphyseal line, indicating growth in the interim. *C*, knee, Oct. 26, 1934, more than three years after the acute illness. The lines of increased density are now several centimeters from the ends of the bones, owing to growth during this time.

LITERATURE

Symptomatology.—A clinical picture characterized by increased intracranial tension, choked disks, external rectus palsies, vomiting, headache and convulsions is particularly apt to occur in children as a result of lead intoxication. Although lead encephalopathy may occur in adults, it is not as common as in children and appears to be less commonly associated with sufficiently increased intracranial tension to be confused with brain tumor. However, that such is not always the case was pointed out as long ago as 1908 by Bramwell,[4] who discussed the differentiation of the two conditions in adults. The differential points that he stressed were (1) evidence of lead poisoning such as a lead line on the gums, anemia, colic and wrist drop, (2) a history suggestive of previous lead poisoning, (3) occupation, (4) the character of the convul-

4. Bramwell, Byrom: The Differential Diagnosis of Intracranial Tumor and Lead Encephalopathy, Clinical Studies (Edinburgh) **7**: 91-96, 1909.

sions and peculiar mental conditions unlike those seen with tumors, and (5) the finding of lead in the urine. It is worthy of note here that Bramwell was dealing with and speaking of lead encephalopathy in adults. Unfortunately, in the main, his differential points are not applicable to children. As has been previously pointed out, evidence of lead poisoning such as the lead line on the gums, anemia, stippled red blood cells, and peripheral neuritis is commonly absent in lead poisoning in children. A history of previous lead poisoning is rarely elicited. Major convulsions are rare phenomena with tumors in the cerebellar fossa in children, and their occurrence should make one hesitate before making such a diagnosis, but in cases 2 and 3 it is seen that major convulsions may be absent in cases of lead encephalopathy. Changes of mentality in children are largely those due to increased intracranial pressure as is true in cases with tumors. The delirium, hallucinations and delusions so frequently seen in lead encephalopathy in adults are rarely observed in the child.

Fig. 5 (case 3).—Skull and ventriculogram, Nov. 17, 1930. There is a very slight separation of the coronal suture. The outline of the lateral ventricles, which is just visible, indicates a normal ventricular system.

That lead intoxication may result in signs of meningeal irritation or in generalized convulsions has been pointed out by Thomas and Blackfan,[6] Blackfan,[7] Strong [8] and Holt.[9]

However, the paper by Suzuki and Kaneko [10] in 1924 describing the Japanese and Manchurian cases of "serous meningitis" in infants arising from the use of lead-containing cosmetic powders by their mothers and the report by McKhann [11] in 1926 of cases of lead encephalopathy in children were the first really to direct attention to the prevalence and the seriousness of this condition in children.

McKhann's first patients suffered from vomiting, headache, stupor and convulsions. He drew attention to the increased cerebrospinal fluid pressure but was not at that time impressed by changes in the optic disks. After further experience with the condition he published his paper of 1932 [8] in which he pointed out that the majority of the symptoms—vomiting, visual disturbances, delirium, stupor, coma, convulsions, often elevated arterial pressure, choked optic disks and separation of the cranial sutures—were due to cerebral edema and increased intracranial pressure. This was a valuable contribution to the complete comprehension of lead encephalopathy in children and shifted attention from the toxic action of lead on the nervous parenchyma to the edema that results from damage to the mesenchymatous elements of the central nervous system, such as the vascular system and the meninges. Other papers [12] in association with Vogt in 1933 and 1934 reemphasized this point. Various writers, including Aub and his co-workers,[13] confirmed the symptomatology as outlined and pointed out that the condition may simulate intracranial neoplasms, as did also Bailey.[14]

The most important recent diagnostic criterion that has been described in this condition in children is the presence of lines of increased density at the ends of the diaphyses of long bones, which are visible with the x-rays. They were recognized and described by Park and his co-workers,[15] Caffey [16] and Vogt.[17] And though in the absence of other confirmatory evidence these lines would be interpreted by few observers as positive evidence of lead poisoning, their presence is very suggestive of the possibility of lead intoxication. There is also the advantage that the existence of such lines of increased density can be easily and quickly determined.

Prognosis.—The mortality from lead poisoning in children is extremely high. Blackfan [7] states that of Stewart's seven patients with convulsions six died, and of his own four patients three died. Holt [9] records that in thirty cases of lead poisoning collected from the literature there were twenty deaths. Aub and his associates [13] state that the literature indicates a mortality of from 25 to 75 per cent in lead poisoning. McKhann and Vogt [12a] state that in forty-five cases of lead encephalopathy in a Boston pediatric hospital there were eleven deaths (24.4 per cent).

Sequelae.—Of equal importance with the mortality is the trail of physical wrecks that lead encephalopathy leaves in its wake. In the forty-five cases of lead encephalopathy recorded by McKhann and Vogt, twelve (26.6 per cent) presented sequelae. These may take various forms. Gowers [5] long ago pointed out the occurrence of a hemiplegia as a result of the disease. Aub and his associates, McKhann and Vogt, and others have reported convulsions, blindness, paralysis, mental deficiency, delirium and melancholia, tremor, speech defects and the like associated with such anatomic changes as cerebral atrophy and internal hydrocephalus. McKhann felt that the sequelae, like the acute signs, could be attributed to the increased intracranial pressure and edema with their attendant

6. Thomas, H. M., and Blackfan, K. D.: Recurrent Meningitis, Due to Lead, in a Child of Five Years, Am. J. Dis. Child. **8**: 377-380 (Nov.) 1914.

7. Blackfan, K. D.: Lead Poisoning in Children, with Especial Reference to Lead as a Cause of Convulsions, Am. J. M. Sc. **153**: 877-887 (June) 1917.

8. Strong, R. A.: Meningitis Caused by Lead Poisoning in a Child of Nineteen Months, Arch. Pediat. 1920, **37**: 532-537 (Sept.) 1920.

9. Holt, L. E., Jr.: Lead Poisoning in Infancy, Am. J. Dis. Child. **25**: 229-233 (March) 1923.

10. Suzuki, T., and Kaneko, J.: Serous Meningitis in Infants Caused by Lead Poisoning from White Powders, J. Orient. Med. 1924, **2**: 55-66, 1924.

11. McKhann, C. F.: Lead Poisoning in Children, Am. J. Dis. Child. **32**: 386-392 (Sept.) 1926.

12. (a) McKhann, C. F., and Vogt, E. C.: Lead Poisoning in Children, J. A. M. A. **101**: 113.-1135 (Oct. 7) 1933. (b) Vogt, E. C., and McKhann, C. F.: Lead Poisoning in Infants and Children, Radiology **22**: 87-92 (Jan.) 1934.

13. Aub, J. C.; Fairhall, L. T.; Minot, Anne S., and Reznikoff, Paul: Lead Poisoning, Medicine **4**: 1-250 (Feb.-May) 1925; Medicine Monographs, Baltimore, Williams & Wilkins Company **7**: 265, 1926.

14. Bailey, Percival: Intracranial Tumors, Springfield, Ill., Charles C. Thomas, 1933.

15. Park, E. A.; Jackson, Deborah, and Kajdi, Laslo: Shadows Produced by Lead in the X-Ray Pictures of the Growing Skeleton, Am. J. Dis. Child. **41**: 485-499 (March) 1931.

16. Caffey, J.: Clinical and Experimental Lead Poisoning: Some Roentgenologic Changes in Growing Bones, Radiology **17**: 937-983, 1931.

17. Vogt, E. C.: Roentgenologic Diagnosis of Lead Poisoning in Infants and Children, J. A. M. A. **98**: 125-129 (Jan. 9) 1932.

impairment of the circulation. It should be pointed out that the anatomic changes in the blood vessels will contribute toward the same end.

COMMENT

Differential Diagnosis.—The confusion of cases such as the ones reported here, particularly the first two, with cases of intracranial tumor is not surprising. The rapidity of onset, the early appearance of vomiting, the absence of definite neurologic changes other than those due to increased intracranial pressure, are typical of certain tumors occurring in the midline of the cerebellum of children. It is true that the majority of such cases usually present considerable uncertainty in walking, such as a staggering gait, but this may be minimal or absent, as case 3 reported by Cushing [26] in 1927 or case 24, reported by Bailey.[27] On the other hand, both cases 1 and 2 reported here presented a slight staggering gait and in case 3 the ataxia observed in walking was thought to be out of all proportion to the foot drop. Such staggering and incoordination in cases of lead encephalopathy may be due to the general debility of the patient or may be the result of degeneration of the large ganglion cells of the cerebellum reported both by Hassin [19] and by Freifeld.[23] Flaccidity (hypotonia) of the extremities is common in midline cerebellar tumors but it was also present in these cases of lead encephalopathy. All the other usual signs of disturbance of cerebellar function (nystagmus, ataxia of the upper extremities and the like) are characteristically absent in cases of midline cerebellar tumors in children and thus are naturally of no value in differentiating these two conditions. It would seem that in many cases from a history and physical examination alone a differential diagnosis would be impossible. In those cases in which a blue line is present along the gums or in which there is an anemia and basophilic stippling of the erythrocytes, lead poisoning will of course be suggested to all observers, but unfortunately these signs are often absent in children. But in those cases in which there is a history of ingestion of lead or of substances that may contain lead, of a rapid onset with marked vomiting and abdominal pain, in which the signs of a localized intracranial lesion are vague or absent, the possibility of lead encephalopathy should be entertained. Such cases will usually show less elevation of the intracranial pressure as evidenced by a less marked separation of the cranial sutures than is usual in cases of cerebellar tumor. Whenever the possibility of lead encephalopathy is being considered in such a case, roentgenograms of the wrists and knees should be made to determine whether lines of increased density are present at the ends of the bones. In this connection it should always be borne in mind that the lead lines may be slight or absent, as in case 3, for the lines indicate the deposition of lead in an inactive form in growing bones, not the presence of lead in a toxic form in the blood stream or brain, and either may be present without the other. It should be stressed that there are no positive criteria of lead encephalopathy in children and only constant vigilance and the use, when indicated, of all the diagnostic methods available will serve to establish the correct diagnosis. Fortunately, as will in a moment be pointed out, the error of diagnosing a case of lead encephalopathy as one of intracranial tumor does not seem to be fraught with grave danger if the proper therapeutic indications are followed.

Treatment.—The therapeutic measures directed at the storage or removal of the lead itself have been very adequately dealt with by numerous recent authors.[28] That phase of the treatment will not be discussed here except to say that in our opinion "deleading" is not only an unnecessary but probably a dangerous procedure in children and should not be attempted except under the most unusual circumstances.

Numerous authors, particularly McKhann, have been impressed by the difficulty of relieving the increased intracranial tension by medical means. The convulsions can often be controlled by intramuscular magnesium sulphate or other methods, but the increased intracranial pressure, little or only temporarily affected by lumbar puncture and hypertonic solutions, continues unabated and results in death in at least one case out of every four and in sequelae in a like number. In less than 50 per cent of the patients under medical management can it be anticipated that they will survive their illness without bad effects.

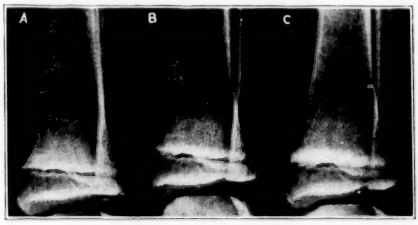

Fig. 6 (case 3).—Right ankle: *A*, Oct. 20, 1930; a faint indefinite line of increased density is present at the end of the tibia. *B*, December 16, after administration of viosterol and calcium lactate for two months; the line of increased density is now distinct and definite. *C*, Feb. 16, 1931; the line is still wider and more dense. It is of course questionable whether this can be spoken of as a "lead line" in view of the therapy.

The present report, limited as it is to three cases, would indicate that every case of lead encephalopathy with increased intracranial pressure should be given the benefit of a cerebellar decompression. The three cases reported here, though recovery occurred in all, are excellent illustrations of that point. Patients 1 and 2, both seriously ill, would have been given a bad prognosis under medical management. With a decompression both rapidly recovered, and in neither is there any trace of any sequel as a result of the illness, whereas in case 3, in which no decompression was made although the intracranial pressure was much less elevated, as shown by the slighter degree of separation of the sutures and the absence of any dilatation of the ventricular system, the recovery was very slow; for weeks the patient was stuporous, her condition growing worse, and for a long time her ultimate recovery

19. Hassin, G. B.: The Contrast Between the Brain Lesions Produced by Lead and Other Inorganic Poisons and Those Caused by Epidemic Encephalitis, Arch. Neurol. & Psychiat. **6:** 268-285 (Sept.) 1921.

23. Freifeld, H.: Veränderungen des Nervensystems bei Bleivergiftung, Virchows Arch. f. path. Anat. **287:** 549-554, 1933.

26. Cushing, Harvey: The Intracranial Tumors of Preadolescence, Am. J. Dis. Child. **33:** 531-584 (April) 1927.

27. Bailey, Percival: Intracranial Tumors, pp. 225-227.

28. In a symposium dealing with lead poisoning, consisting of the following papers:
Lanza, A. J.: Epidemiology of Lead Poisoning, J. A. M. A. **104:** 85 (Jan. 12) 1935.
Aub, J. C.: The Biochemical Behavior of Lead in the Body, p. 87.
Kehoe, R. A.; Thamann, Frederick, and Cholak, Jacob: Normal Absorption and Excretion of Lead, p. 90.
Jones, R. R.: Symptoms in Early Stages of Industrial Plumbism, ibid. **104:** 195 (Jan. 19) 1935.
Gray, Irving: Recent Progress in the Treatment of Plumbism, p. 200.
Belknap, E. L.: Control of Lead Poisoning in the Worker, p. 205.

was actually in doubt. Surely if cases 1 and 2 are any indication at all, her recovery would have been much more rapid with a decompression.

As to what form of decompression is most suitable, we have no information. In both of our cases a suboccipital (cerebellar) decompression was made. It has the advantage that the cerebellum is exposed in those cases in which the question of cerebellar tumor is not entirely settled, and it has the added value of leaving no unsightly scar or protrusion. It is obviously possible that a subtemporal decompression could prove as effective a mode of treatment. If so, it would have the advantage that it is a little more easily and quickly made but the disadvantage of the scar and of an obvious defect in the temporal bone. It is doubtful whether in competent hands the one is any more dangerous than the other in cases of lead encephalopathy.

SUMMARY

In two of three cases of lead encephalopathy in children with increased intracranial tension simulating cases of intracranial tumor, a suboccipital decompression was made. Both children recovered promptly and completely. In the third, in which the intracranial pressure was less elevated, no decompression was made and medical management alone was used. This child had a prolonged and stormy course but also ultimately recovered. From these experiences and from data taken from the literature, it is concluded that:

1. The differentiation of lead encephalopathy and midline cerebellar tumors in children from the history and physical signs alone is difficult and may be impossible.

2. Such factors as the possible ingestion of lead, rapid onset with vomiting and abdominal pain, and only moderately increased intracranial pressure should warn the clinician of the possible diagnosis of lead encephalopathy.

3. The easiest and most rapid method of rendering probable the diagnosis of lead encephalopathy is the demonstration of the presence of lines of increased density at the ends of the long bones. The diagnosis may then be established by demonstrating the presence of lead in the blood.

4. Medical management of lead encephalopathy is notoriously unsatisfactory and results in a high mortality and numerous and serious sequelae.

5. Surgical decompression of the intracranial cavity offers a logical means of producing a prompt and complete relief of symptoms with less danger of sequelae.

ABSTRACT OF DISCUSSION

DR. TRACY J. PUTNAM, Boston: The authors have called attention to an important point in the differential diagnosis. I have seen at the Boston Children's Hospital several patients with encephalitis due to lead poisoning whose symptoms closely simulated those of tumor. The differential diagnosis in such cases is one to which insufficient attention has been paid. In some of the cases at the Children's Hospital the intracranial pressure has been raised even more than I should judge was observed in the patients whose histories Drs. Bucy and Buchanan have reported. The sutures have been widely spread and the intracranial pressure as measured with a spinal manometer has been found to be over a 1,000 mm. of water. A few of these patients have been operated on and decompression has been effected. In severe cases of increased suboccipital pressure, decompression is apparently inadequate. I believe there are cases, however, in which benefit would be obtained by decompression. I am skeptical as to whether swelling of the brain itself would be substantially reduced by suboccipital decompression, although this is strongly suggested in the cases of Drs. Bucy and Buchanan.

DR. HANS REESE, Madison, Wis.: Four years ago I examined a boy, 5 years of age, who presented the characteristic signs of cerebellar tumor. I was not able to trace the syndrome to an intoxication or an infection and was not satisfied with the diagnosis of tumor, so I referred him to the neurologic department of the University of Chicago. Suboccipital decompression was performed but, instead of a tumor, hemorrhagic arachnoiditis was found. Uneventful recovery followed this operation. The boy is alert, steady and quick, but an interesting feature is that within the last four years he has not grown. Clinical examination shows that he is normal and well nourished but undersized. His head is somewhat large but not hydrocephalic. After hearing this paper, I am of the opinion that in this case the possibility of encephalopathy due to lead poisoning was overlooked. I shall study the epiphyseal region to see if lead lines are evident.

DR. ROY GRINKER, Chicago: Since attention has been drawn to the possibility of lead poisoning in the etiology of the rarely diagnosed cases of serous arachnoiditis, I have been impressed by the fact that the pathologic process in encaphalopathy due to lead poisoning—changes in the ganglion cells, swelling of the brain, meningeal proliferation and secondary hydrocephalus—are often found in children with a condition which Stone and I have called toxic encephalitis. These pathologic changes are so similar, occur so frequently in children and lead to such similar sequelae that not only must evidence of lead poisoning be searched for as a possible etiologic factor in these cases in which a tumor is not present but in which simulating symptoms are noted and which have therefore frequently been called cases of pseudotumors, but in addition one must be careful not to miss some previous acute infection that may have been responsible for the pathologic changes which later cause a rise in the intracranial pressure and thus confuse the clinical picture.

DR. E. D. FRIEDMAN, New York: May I ask how the authors would explain the presence of the changes in the fundus noted in the last case?

DR. L. H. LOESER, Newark, N. J.: May I ask the authors to give further information as to the lead line in the bones? At what age does it appear? Is it present in adults?

DR. PAUL C. BUCY, Chicago: The patient whom Dr. Reese mentioned is one in whom we were interested. However, the roentgenograms taken at the clinic gave no clue as to whether or not it might have been a case of lead encephalopathy, and unfortunately we were unable to follow the patient further. I do not believe that the retardation of growth which occurred in Dr. Reese's case was due to the deposition of lead along the epiphyseal lines. As noted in case 2, such deposition does not retard growth. I am inclined to feel that the retardation of growth in his case was due to the intracranial changes produced by the disease. Although dilatation of the ventricular system is commonly associated with increased intracranial pressure, its presence is by no means essential. It is well known that edema of the brain occurs in encephalopathy due to lead poisoning and I am inclined to believe that such edema is an adequate explanation of the papilledema and increased intracranial pressure that were noted in the third case. The lead line occurs only in children because it is associated with the laying down of calcium in growing bone. It is of no value as a diagnostic sign in adults.

Honored by Severe Criticisms.—Bayle's contribution met with the greatest success that can come to any medical contribution in that it led to widespread consideration and discussion. In fact, the author was honored by many severe criticisms, not to mention personal attacks. As a result, the question of chronic arachnitis became a lively issue in the medical world, and from this original description of six cases and the conclusions drawn the subject has grown by addition to the present state of knowledge concerning dementia paralytica.—Moore, Merrill, and Solomon, H. C.: Contributions of Haslam, Bayle, and Esmarch and Jessen to the History of Neurosyphilis, *Arch. Neurol. & Psychiat.* **32**:804 (Oct.) 1934.

RECENT ADVANCES IN THE STUDY OF INFLUENZA

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The name "influenza" usually conjures up a picture of the disease as it appeared during the pandemic of 1918-1919—a disease of widespread distribution and protean manifestations, characterized by rapid dissemination, a high frequency of complicating pneumonia, and a high mortality. In sharp contrast, one may present the milder epidemics that occur from year to year in different communities, usually limited in their scope, severity and complications. The number of cases that occur in these mild epidemics depends, to a certain extent, on the number of clinically similar infections that are included under the diagnosis of influenza.

THE DIAGNOSIS OF INFLUENZA

In fact, the lack of sharp differential features has rendered it difficult to separate influenza as a well defined clinical entity from many other mild infections of similar symptomatology that may invade a community. Thus the term "influenza" has been carelessly applied to various vague diseases of comparatively high morbidity which are associated with chills and generalized aches and pains and are of brief duration. A striking example of this tendency was reported from South America two years ago.[1] An epidemic of a mild nature, which was called influenza or grip, invaded a localized area in Brazil. When studies of the immunity reactions of individuals in this area were made, it was found that the disease was, in fact, yellow fever.

One may adopt, as requisites for the diagnosis of influenza, certain criteria such as sudden onset with constitutional symptoms, chilliness, fever, myalgia, headache, mild respiratory symptoms without coryza, the presence of leukopenia, and a course of from two to three days followed by considerable asthenia and exhaustion. These may serve as a working basis but are insufficient to exclude other entirely different diseases that exhibit a similar clinical picture.

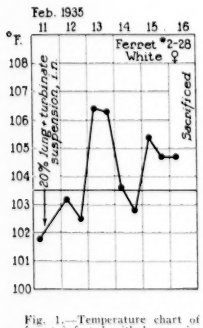

Fig. 1.—Temperature chart of a ferret infected with human influenza virus.

THE PROBLEM OF ETIOLOGY

A comparable state of uncertainty has prevailed in regard to the causative agent of influenza. Many different bacteria have been implicated, particularly Haemophilus influenzae and Bacterium pneumosintes, but in no case has the evidence been sufficiently convincing to permit of their acceptance as the specific causative factors. Certain scattered data have previously been presented which suggest that the etiologic agent belongs to that group of ultramicroscopic infectious agents called filtrable viruses. Although suggestive, the demonstration of a filtrable virus has not been conclusive, since repeated attempts by other workers to transmit the disease experimentally have yielded negative results.

RECENT STUDIES OF OTHER RESPIRATORY DISEASES IN MAN AND ANIMALS

In recent years, however, three different series of studies have been carried on which have again increased the interest in the etiology of influenza. These three series of investigations have been concerned with diseases involving the respiratory tract, which in each case has permitted of study of a disease occurring in its natural host.

Fig. 2.—The lung of a ferret infected with human influenza virus; posterior aspect; complete consolidation of left lower lobe.

The first of the series comprises the studies undertaken by Dochez,[2] Shibley, Kneeland and Mills, and Long and his co-workers[3] on the common cold. Briefly, the results of the investigation indicate that the common cold in man is produced by a filtrable virus which can also initiate a similar condition in the chimpanzee, and that the virus can be grown in artificial mediums and after cultivation still maintains the capacity to induce common colds in human individuals.

The second study, carried out by Laidlaw and Dunkin,[4] was concerned with dog distemper, a highly infectious respiratory disease. These investigators, in addition to their work with dogs, the natural hosts, succeeded in transferring the disease to ferrets and were enabled thereby to study the disease experimentally in a stock known to be free from natural infection and maintained under conditions of rigid quarantine. They were able to establish the fact that this malady is caused by a filtrable virus.

The third set of investigations is that of Shope,[5] relating to a respiratory disease of swine, which, so far as is known, first made its appearance at the time

From the Hospital of the Rockefeller Institute.
Read before the New York County Medical Society, Feb. 25, 1935.

1. Soper, F. L., and de Andrade, A.: Studies of the Distribution of Immunity to Yellow Fever in Brazil: II. The Disproportion Between Immunity Distribution as Revealed by Complement-Fixation and Mouse-Protection Tests and History of Yellow Fever Attack at Cambucy, Rio de Janeiro, Am. J. Hyg. **18:** 588 (Nov.) 1933.

2. Dochez, A. R.: A Limited Consideration of Certain Aspects of Acute Infection of the Respiratory Tract, Medicine **12:** 245 (Sept.) 1933.

3. Long, P. H., and Doull, J. A.: Etiology of Acute Upper Respiratory Infection (Common Cold), Proc. Soc. Exper. Biol. & Med. **28:** 53 (Oct.) 1930. Long, P. H.; Doull, J. A.; Bourn, J. M., and McComb, E.: Etiology of Acute Upper Respiratory Infection (Common Cold), J. Exper. Med. **53:** 447 (Dec.) 1931.

4. Dunkin, G. W., and Laidlaw, P. P.: Studies in Dog Distemper: I. Dog Distemper in the Ferret, J. Comp. Path. & Therap. **39:** 201 (Sept.) 1926; II. Experimental Distemper in the Dog, ibid. p. 213. Laidlaw, P. P., and Dunkin, G. W.: III. The Nature of the Virus, ibid. p. 222.

5. Shope, R. E.: Swine Influenza: I. Experimental Transmission and Pathology, J. Exper. Med. **54:** 349 (Sept.) 1931. Lewis, P. A., and Shope, R. E.: II. A Hemophilic Bacillus from the Respiratory Tract of Infected Swine, ibid. p. 361. Shope, R. E.: III. Filtration Experiments and Etiology, ibid. p. 373; Studies on Immunity to Swine Influenza, ibid. **56:** 575 (Oct.) 1932.

of the influenza pandemic of 1918-1919. This disease has been called swine influenza, or hog flu. It is characterized by fever, loss of appetite and weight, cough, respiratory distress and pulmonary consolidation, but it is of comparatively low mortality. Shope, in a series of brilliant studies, was able to demonstrate that the disease was produced and transmitted through contact infections by a filtrable virus in symbiosis with a bacterium of the group to which the human types of Haemophilus influenzae belong. The bacillus alone injected into the nose of a hog, except in rare instances,

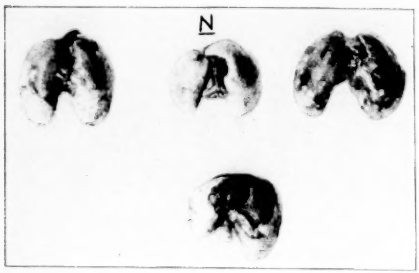

Fig. 3.—Lungs of mice infected with human influenza virus in comparison with normal mouse lung (*N*).

produced no effect; the filtrable virus alone produced a mild and, at times, unrecognizable infection but one which nevertheless was followed by a firm immunity against infection by the two agents combined. Furthermore, it was possible, by the subcutaneous injection of the filtrable agent into swine, to induce a state of immunity that protected against infection when the virus and influenza bacillus were injected together into the nose of the hog.

Studies such as these have served to heighten the probability that similar conditions may obtain in other epidemic respiratory infections, especially those of man.

TRANSMISSION TO FERRETS OF A FILTRABLE VIRUS FROM HUMAN INFLUENZA IN ENGLAND

In 1933 Smith, Andrewes and Laidlaw [6] instilled into the noses of ferrets filtered nasopharyngeal washings obtained from human patients during the acute stage of influenza. Two days after inoculation the ferrets became ill with fever, apathy, loss of appetite and nasal catarrh. The ferrets were killed on the third or fourth day after the onset of fever, and, with emulsions of the nasal turbinate bones of such animals, these investigators were able to transmit the disease to other ferrets. The only pathologic change that they found in the infected animals was inflammation of the nasal mucous membranes. Ferrets that recovered from the disease were found to be immune to reinfection. The serum of these recovered animals contained antibodies that were capable of neutralizing the action of the infective agent when the serum and infectious material were mixed and then inoculated into a susceptible ferret. Similar antibodies were detected in the serum of men convalescent from influenza and in the serum of other human individuals as well. The active agent was found to be a filtrable virus, and the addition of various bacteria caused no definite difference in the experimental disease.

6. Smith, Wilson; Andrewes, C. H., and Laidlaw, P. P.: Virus Obtained from Influenza Patients, Lancet **2**: 66 (July 8) 1933.

EXPERIMENTAL SWINE INFLUENZA IN FERRETS

In addition, the British workers were able to transmit the virus of swine influenza to ferrets, producing a disease indistinguishable from that caused by the human strain of virus. Shope [7] was able to confirm their observations regarding swine influenza in ferrets. Furthermore, he found that, when suspensions of finely ground lung of infected hogs or bacteria-free filtrates of such suspensions were injected intranasally into anesthetized ferrets, there developed, in addition to the inflammation of the nasal mucous membranes, involvement of the lung itself. The pulmonary involvement was of lobar distribution, firm and markedly edematous. The alveolar walls were thickened with many mononuclear and polymorphonuclear cells, while in the alveolar spaces the exudate was sparse and composed primarily of mononuclear cells. After repeated passages in ferrets the virus still retained its infectivity for swine, producing characteristic swine influenza when mixed with swine influenza bacilli, while in the experimental disease in ferrets no bacterial component was required. The serum of recovered swine or ferrets was found to be capable of inhibiting the activity of the virus.

RECOVERY OF A FILTRABLE VIRUS FROM HUMAN INFLUENZA IN AMERICA [8]

With the results of these studies as a background, during the winter of 1933-1934 I inoculated material from various human respiratory infections into the nasal passages of ferrets, but, with the exception of one

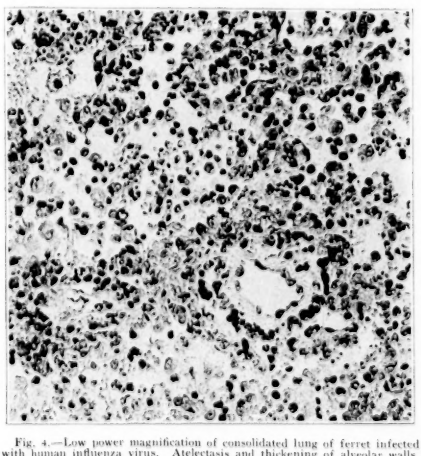

Fig. 4.—Low power magnification of consolidated lung of ferret infected with human influenza virus. Atelectasis and thickening of alveolar walls, edema fluid and scanty exudate in alveolar spaces. Early perivascular round cell infiltration.

instance of definite bacterial origin, I was unable to establish any disease in the animals.

In the early autumn of 1934, however, a widespread epidemic of influenza occurred in Puerto Rico. Through the kindness of physicians of the International Health Board, sputum was obtained from patients dur-

7. Shope, R. E.: The Infection of Ferrets with Swine Influenza Virus, J. Exper. Med. **60**: 49 (July) 1934.

8. Francis, Thomas, Jr.: Transmission of Influenza by a Filtrable Virus, Science **80**: 457 (Nov. 16) 1934.

ing this epidemic. The sputum was placed in sealed bottles of 50 per cent glycerin, packed in a vacuum jug with ice and shipped to New York by air mail. The materials were received from three to five days after collection. The sputum was washed free from glycerin and emulsified with Locke's solution; the emulsions were inoculated into the nasal passages of

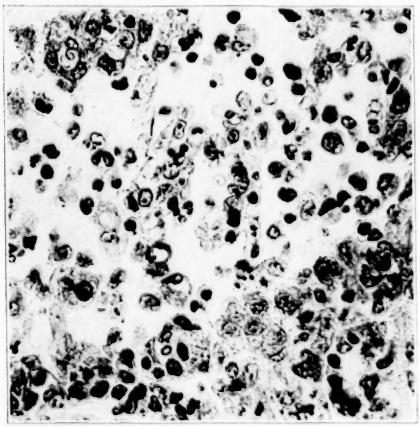

Fig. 5.—High power magnification of same area shown in figure 4. The predominant cell in the exudate is a large pale-staining mononuclear cell resembling the alveolar phagocytes.

ferrets lightly anesthetized with ether. On the second day after inoculation, fever developed in all the animals. Three days later one of these was killed and the lungs and turbinates were removed and ground in a mortar with sand and meat infusion broth. Part of the material was centrifugated and filtered through a Berkefeld V filter. Two ferrets were given the unfiltered suspension intranasally; another was given the bacteria-free filtrate by the same route. All three animals were taken sick, and with the virus recovered from these animals it has been possible to transfer the disease in serial passages from ferret to ferret by means of suspensions of filtrates of either ground lung or turbinate.

In the first few passages of the virus through ferrets the disease is characterized by a diphasic type of fever and mild apathy, but little else (fig. 1). After a few passages, however, in the lungs of ferrets that are killed on the fourth or fifth day, bluish consolidation of the lower lobes is usually noted, and subsequently similar involvement of the lungs has almost always occurred after intranasal infection. In animals with pulmonary involvement the disease is more severe (fig. 2). Their respirations are rapid, somewhat jerky and labored, and at times moaning in character. A short dry cough may be noted. There may be a watery nasal and conjunctival discharge. The animals, usually alert and active, are apathetic and lie quiet in their cages, eating little. After from five to six days, recovery begins and the animal rapidly regains an apparently normal interest in food and in its surroundings. Recovery is almost invariably the rule.

On the fourth day after the original material was obtained from Puerto Rico, one of the laboratory assistants was taken sick, and two days later another assistant was also taken sick, both with symptoms typical of influenza. The throat washings obtained from these two patients at the height of the disease were inoculated into ferrets, and a characteristic experimental disease was produced. These observations indicate the infectiousness of the material for man, since influenza was not known to be prevalent in the community at that time.

THE EXPERIMENTAL DISEASE IN MICE

With filtrates of the sputum from Puerto Rico, and of the washings of the contact cases, attempts were made to establish the infection in mice, but without success. Different groups of mice, under ether anesthesia, were also inoculated intracerebrally, intranasally and intraperitoneally with filtrates of suspensions of lung from the different passage ferrets. We finally noted, in one group of mice that were killed four days after intranasal inoculation, some small areas of reddish blue consolidation in the upper portions of the lungs. The involved areas were ground with sand and bouillon, and the centrifugated suspension was then injected into the nasal passages of other mice. By repeating this process through several passages in mice, it was finally possible, with bacteria-free suspensions of the mouse lung, or with Berkefeld filtrates, consistently to induce this reaction in mice. The disease in mice, after intranasal infection, is primarily one of the respiratory tract and essentially of the lungs. The rapidity of the course of the disease

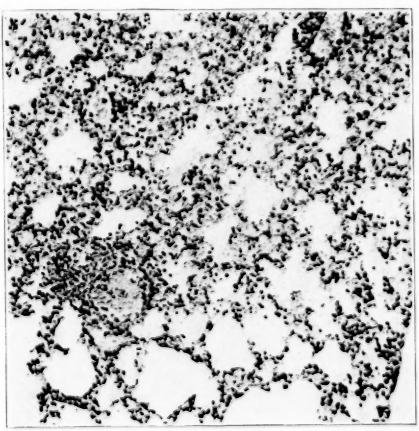

Fig. 6.—Low power magnification of mouse lung at margin of consolidated area. In the upper part there is a great amount of edema fluid, partial atelectasis and early perivascular cuffing. The lower portion shows uninvolved lung with compensatory emphysema.

depends, to a certain extent, on the concentration of the infectious agent in the inoculum (fig. 3). After the intranasal instillation of a 5 per cent suspension of lung tissue, the mice begin to sicken on the second or third day; they are quieter, their coats become ruffled, and they huddle together and eat but little. The respirations become exaggerated, labored and audible, the eyes become wet and staring, and the animal dies in from four to eight days.

At autopsy, the lungs are almost completely involved. They are distended and a reddish blue; the surfaces are smooth and glistening, and when the lungs are removed from the body considerable froth exudes from the trachea. In the earlier stages, the involvement is most marked in the dorsal aspects of the upper lobes and about the roots of the lobes. It has been possible to carry the disease through many transfers in mice, with only an occasional survivor. From the lungs of the mice one can in turn infect the ferret, producing a characteristic illness.

While these studies were in progress, Andrewes, Laidlaw and Smith [9] reported independently that they had been successful in establishing the human and swine influenza viruses in mice with a resulting pathologic picture similar to that which we have described.

MICROSCOPIC PATHOLOGIC CHANGES OF THE EXPERIMENTAL DISEASE

Microscopically, the changes in the lungs of both the ferrets and the mice are similar to those described by Shope [7] in the lungs of swine and ferrets with swine influenza. There is a marked thickening and proliferation in the alveolar walls; there is an atelectatic appearance in some areas, and the cellular exudate is comparatively scanty, while considerable edema fluid may be present. The type of cell, in contrast to that seen in the ordinary bacterial infections, is primarily the large mononuclear, and there is some infiltration of small round cells about the blood vessels (figs. 4, 5 and 6).

ADDITIONAL STUDIES

The results of filtration and cultural studies indicate that the infective agent of epidemic influenza is a filtrable virus. The infection has not been transmitted readily by contact from infected to normal animals or by other routes than the respiratory tract.

We have succeeded in recovering a similar infectious agent from the nasal washings of patients during the recent mild epidemics of influenza in New York and Philadelphia. The studies with these strains have not been carried out extensively as yet, but the course of the experimental disease in ferrets and mice is much the same. The blood of patients suffering from influenza, in spite of the generalized symptoms, has not been found to infect the mouse or the ferret, nor has it been possible with the throat washings of patients to transfer the infection directly to mice.

SUMMARY AND CONCLUSIONS

The results of these studies, together with those of Andrewes, Laidlaw and Smith, have succeeded in establishing the fact that one, at least, of the mild interpandemic diseases called influenza is causally related to a filtrable virus and can be transmitted experimentally to mice and ferrets. The disease in both species of animals chiefly involves the respiratory tract and produces a typical pulmonary consolidation. A human disease studied in two widely separate parts of the world, and in each instance considered typical influenza, has thus been found to exhibit similar characteristics in experimental animals. The picture of the infection in the animals may serve not only as a guide for further investigations of influenza but also as a basis for differentiating influenza from other epidemic diseases which, at the present time, because of a lack of differential criteria, are probably included in the category of influenza.

9. Andrewes, C. H.; Laidlaw, P. P., and Smith, Wilson: Susceptibility of Mice to Viruses of Human and Swine Influenza, Lancet **2**: 859 (Oct. 20) 1934.

AURICULAR FIBRILLATION IN HYPERTHYROID PATIENTS

PRODUCED BY ACETYL-β-METHYLCHOLINE CHLORIDE, WITH OBSERVATIONS ON THE RÔLE OF THE VAGUS AND SOME EXCITING AGENTS IN THE GENESIS OF AURICULAR FIBRILLATION

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AND
H. E. HOFF, PH.D.
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Auricular fibrillation is a serious cardiac irregularity which results from the onset of one or more circus movements in the auricular musculature (Lewis). The factors that initiate the circus movements are not too well understood. In the following study these factors have been investigated, and it became clear that auricular fibrillation can be produced in hearts when they are subjected to the combined action of an exciting agent and overactivity of the vagus nerve.

THE ACTION OF THE VAGUS

Our first intimation of the nature of the physiologic mechanism involved in auricular fibrillation was obtained while observing the effects of acetyl-β-methylcholine chloride on a hyperthyroid patient in whom a tachycardia had suddenly developed. As a matter of fact, the patient was really suffering from auricular flutter, and administration of the drug converted the flutter into auricular fibrillation. The electrocardiogram obtained from this patient is reproduced in figure 1 and in the control record shows auricular flutter with a 2:1 block. After the injection of 50 mg. of acetyl-β-methylcholine chloride, the block gradually increased to 4:1; three mintues later the block was 5:1, the auricular complexes began to fragment, and a coarse fibrillation was established and shortly replaced by fine auricular fibrillation. An hour and a half later, when the effect of the injection might be expected to have worn off, a normal slow supraventricular rhythm spontaneously reappeared (fig. 1 *F*). Figure 1 *G* is a reproduction of the electrocardiogram taken after a lapse of two days.

The increasing auriculoventricular block and the slowing of the ventricular rate are typical depressor effects and were to be expected from the well known action of the drug. The increase in the auricular rate from 316 to more than 600 was, however, an entirely unexpected finding. It was obvious, however, that the vagus substance promoted the change from auricular flutter to auricular fibrillation.

The next logical step was to find out whether acetyl-β-methylcholine chloride might play a similar rôle in converting the normal heart mechanism in hyperthyroid patients into auricular fibrillation. Accordingly, five patients at the Hospital of St. Raphael in New Haven were selected for study. Of these, one was doubtfully hyperthyroid, having a basal metabolic rate of plus 13. The other four were clearly defined hyperthyroid patients, with basal metabolic rates ranging from plus 26 to plus 48. All five received acetyl-β-methylcholine chloride in doses of 0.75 mg. per kilogram of body weight. Continuous electrocardiograms were taken in each case after the administration of the drug.

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All five patients showed marked vagal as well as generalized parasympathetic effects similar to those described by Starr and his co-workers in man,[1] and by us in the infrahuman primates.[2] Accompanying these symptoms there was a rapid, and, in two patients, a profound drop in the blood pressure, requiring a subcutaneous injection of atropine sulphate, $^1/_{100}$ grain (0.0006 Gm.), to terminate the further action of the drug. In these two patients evidences of myocardial ischemia appeared and were recognized by a displacement of the ST segment of the ventricular complex (fig. 2). In a series of similar studies made in a group of normal patients and animals, such a marked drop of the blood pressure was never observed with corresponding doses of the drug. Slowing of the heart rate and a partial auriculoventricular block took place in all five patients. Flushing was replaced at regular intervals of about four minutes by general peripheral vasoconstriction. These periods were found to coincide with transient increases in the heart rate. The maximum effects were reached from eight to ten minutes after injection and recovery was complete from forty-five minutes to two hours later.

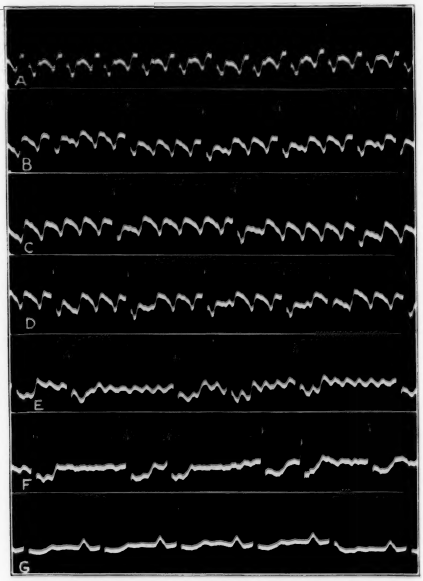

Fig. 1.—Lead 2 in Mrs. S., aged 46, with a basal metabolic rate of +42. Auricular flutter for two days, refractory to digitalis. Electrocardiograms taken at intervals of five minutes: *A*, control; auricular flutter with 2:1 rhythm. *B*, five minutes after a subcutaneous injection of 50 mg. of acetyl-β-methylcholine chloride; 4:1 block. *C*, 6:1 block. *D*, beginning fragmentation of P waves. *E*, coarse auricular fibrillation. *F*, fine auricular fibrillation. *G*, resumption of normal rhythm one and one-half hours after injection of the drug.

In the four definitely hyperthyroid patients the drug also produced a short period of auricular fibrillation, but this was not observed in the doubtful case. Auricular fibrillation appeared as the effect of the drug approached a maximum, while the normal mechanism reappeared from five to twenty minutes later (fig. 3).

From these observations it became clear that the drug played a predominant rôle in the production of auricular fibrillation in hyperthyroid patients having normal cardiac mechanism. Since the acetylcholine

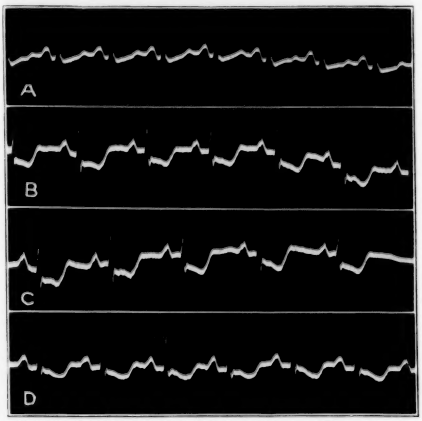

Fig. 2.—Lead 2 in Mrs. W.: *A*, control. *B*, one minute after injection of 50 mg. of acetyl-β-methylcholine chloride; slowing of large S wave, displacement of ST segment and inversion of the T wave. *C*, two minutes after injection. *D*, beginning recovery after injection of 0.01 Gm. of atropine.

derivative reproduces the same effects on the pacemaker and auricle of the heart as stimulation of the vagus nerves,[2] it became clear that one factor in the spontaneous production of auricular fibrillation is the action of the vagus nerves on the heart.

Vagal excitation alone rarely causes auricular fibrillation. We have administered acetyl-β-methylcholine chloride to several normal individuals and to more than a hundred cats and monkeys and have never observed auricular fibrillation, nor was it reported by Starr and his co-workers in their studies on man. Eccles and Hoff [3] observed a few extrasystoles at a rapid rate at the pacemaker following weak tetanic stimulation of the vagus of a cat but no true fibrillation, but, when Lewis, Drury and Iliescu [4] added another factor such as faradic stimulation to the auricles of a dog during vagal stimulation, they observed incipient auricular fibrillation. They also obtained transient auricular fibrillation by faradic stimulation of the auricles alone. However, Eccles and Hoff have shown that in such instances local vagal ganglions are very likely to be stimulated even by very weak currents, in this way probably adding the vagal factor.

THE SECOND FACTOR

Thyroxine.—The production of auricular fibrillation by the injection of acetyl-β-methylcholine chloride in the hyperthyroid patient and the failure to produce this disorder in the normal patient with the same or even

1. Starr, I., Jr.; Elsom, K. A.; Reisinger, J. A., and Richards, A. N.: Acetyl-β-Methylcholin Action on Normal Persons with a Note on Action of Ethyl Ether of β Methylcholin, Am. J. M. Sc. **186**: 313-323 (Sept.) 1933.

2. Hoff, H. E., and Nahum, L. H.: The Prevention of Ventricular Fibrillation Following Electric Shock of Low Voltage by the Injection of Acetyl-β-Methylcholine Chloride, Am. J. Physiol. **110**: 675-680 (Jan.) 1935.

3. Eccles, J. C., and Hoff, H. E.: The Rhythm of the Heart Beat: III. Disturbance of Rhythm Produced by Early Premature Beats, Proc. Roy. Soc. Med., London, s. B. **115**: 352-368 (July) 1934.

4. Lewis, Thomas; Drury, A. N., and Iliescu, C. C.: Further Observations upon the State of Rapid Reexcitation of the Auricles, Heart **8**: 311-339 (Aug.) 1921.

larger doses of this drug makes it seem obvious that the excessive thyroxine present in the former case must in some manner account for the auricular fibrillation that is produced. Hearts under the influence of excessive amounts of thyroxine are stimulated so that they beat rapidly and also show increase in the rate of conduction and force of contraction.[5]

Thyroxine, therefore, might be considered an exciting agent on the heart. The widespread occurrence of auricular fibrillation in other than hyperthyroid persons indicates that agents other than thyroxine may operate with the vagus factor to induce and maintain this disorder. For purposes of exposition we propose to call this the E factor.

Electric Shock.—The essential features of the effect of acetyl-β-methylcholine chloride on cats shocked electrically have been reported incidentally in a different connection [2] and may be stated briefly: In an animal given a preliminary injection of 10 mg. per kilogram of acetyl-β-methylcholine chloride, electric shock with a 110 volt alternating current of short duration invariably produced auricular fibrillation. This condition lasts usually about from one and one-half to two hours, but with weaker shocks a normal rhythm returned in from fifteen to forty minutes.

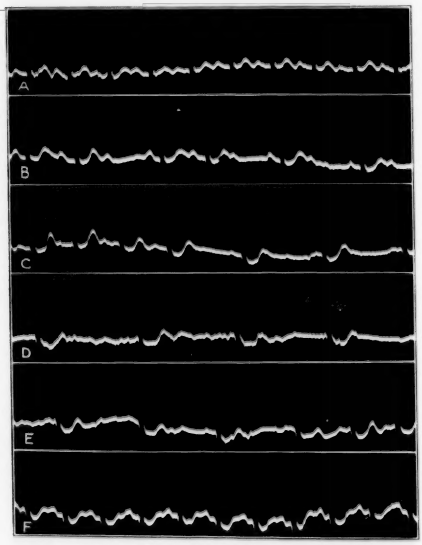

Fig. 3.—Lead 2 in Mrs. C., aged 32, weighing 53 Kg., with a basal metabolic rate of +48. Records at an interval of five minutes: *A*, control. *B*, five minutes after injection of 50 mg. of acetyl-β-methylcholine chloride; partial block. *C*, fragmentation of *P* wave and development of auricular fibrillation. *D*, fully established auricular fibrillation. *E*, transition back to normal rhythm. *F*, fully established normal mechanism.

In most of our experiments the drug was administered first and the shock given from fifteen to twenty minutes later, but in some studies auricular fibrillation was also produced by delivering the shock first and following it with acetyl-β-methylcholine chloride within a very few minutes (fig. 4).

It is apparent that electric shock, just as thyroxine, may, when combined with the vagus factor, produce auricular fibrillation.

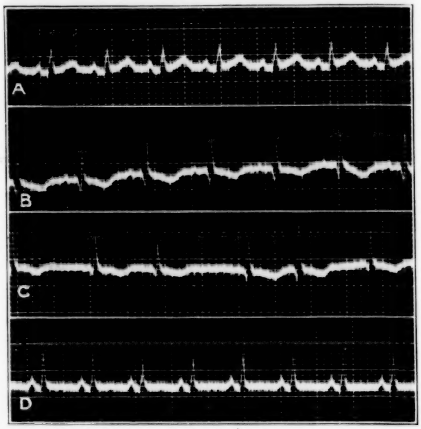

Fig. 4.—Lead 2 in cat, weighing 2.5 Kg., under amytal anesthesia: *A*, control, *B*, ten minutes after a subcutaneous injection of 25 mg. of acetyl-β-methylcholine chloride. *C*, immediately after an electric shock from a 110 volt alternating current with a duration of two and one-half seconds. *D*, resumption of normal rhythm an hour after *C*. Note the presence of *Q* wave in *B* and *C* and inversion of the *T* wave.

The disorder was of a temporary nature in the electrically shocked cats as well as in the hyperthyroid patients, although of shorter duration in the latter. The hyperthyroid subjects either were able to antagonize the action of the vagus substance more readily or received a relatively smaller dose.

It is interesting to note that in our experiments auricular fibrillation developed without passing through the stage of flutter, nor did we observe flutter when the fibrillation passed away, although almost continuous electrocardiograms were made. Flutter, therefore, is apparently not an essential intermediate stage in passing to or from fibrillation.

COMMENT

In these studies auricular fibrillation is shown to result when an increased quantity of the vagus substance acts on the heart in association with some other factor (E), such as electric shock or thyroxine. The degree of vagus activity is evidently of considerable importance since in the hyperthyroid patients the disorder occurred only when additional depressor effects produced by the injection of acetyl-β-methylcholine chloride were added to those already in existence. The spontaneous development of this disorder in hyperthyroid patients must therefore occur when increased depressor effects develop. Since many factors may lead to continued reflex cardiodepressor stimulation and since some individuals exist who are naturally vagosensitive,[6] the necessary quantity of this factor may readily develop in the course of disease. How the

5. Yater, W. M.: The Tachycardia, Time Factor, Survival Period, and Seat of Action of Thyroxine in the Perfused Hearts of Thyroxinized Rabbits, Am. J. Physiol. **98**: 338-343 (Sept.) 1931. Priestley, J. T.; Markowitz, J., and Mann, F. C.: The Tachycardia of Experimental Hyperthyroidism, Am. J. Physiol. **98**: 357-362 (Sept.) 1931.

6. Weiss, Soma, and Baker, J. P.: Carotid Sinus Reflex in Health and Disease: Its Rôle in Causation of Fainting and Convulsions, Medicine **12**: 297-354 (Sept.) 1933.

vagus contributes to the initiation of auricular fibrillation is not apparent from these studies. It is probable, however, that its chief function is to decrease the refractory period of the auricle, thus permitting the initiation of circus movements.[7]

The manner in which the E factor thyroxine—or electric shock (in these studies)—acts in the production and maintenance of this disorder is also not completely clear at this time. The only factor in common between these agents is their property of exciting the myocardium.

Whether there exists a reciprocal relationship between the vagus and the E factor, more of one requiring less of the other in order to induce auricular fibrillation, cannot be answered from these experiments. It is interesting to note that in the ventricles a reciprocal relationship has been found to exist between electric shock and epinephrine.[8]

From the clinical point of view the spontaneous development of auricular fibrillation may now be explained by the simultaneous action on the heart of the vagus and an E factor.

In hyperthyroidism the overactivity of the vagus may develop reflexly from the tachycardia and growing hypertension so often found in these patients. Furthermore, we believe that increased sensitivity to the vagus substance naturally exists in such patients, for two of our subjects suffered severe reactions from normal doses of acetyl-β-methylcholine chloride, and it is well known that hyperthyroid patients exhibit many parasympathetic symptoms such as sweating, flushing of the skin and gastro-intestinal hyperactivity. When the thyroxine effects on the heart reach a certain stage, superimposed vagal overactivity will precipitate auricular fibrillation.

The proper combination of vagus and thyroxine may not and probably does not always exist. This is particularly true when the nerve effects are variable, in which case auricular fibrillation might occur in paroxysms, a phenomenon very common in hyperthyroid patients and most frequent immediately after operation when large amounts of thyroxine are suddenly released into the blood stream.

Apart from hyperthyroidism, auricular fibrillation is found to occur commonly in mitral stenosis, hypertension and congestive heart failure. In these conditions also the explanation for the disorder suggests itself. In mitral stenosis the distention of the auricle leads to an increase in the resting tension of the fibers which, as in skeletal muscle [8] and nerve,[9] may appear in abnormal hyperexcitability. Stretch may therefore be an E factor in mitral stenosis. Active rheumatic infection might also serve as an E factor, since de la Chappelle [10] found a high incidence of active inflammation in the auricles of patients suffering from mitral stenosis in whom auricular fibrillation developed. At some stage of the disease, should overactivity of the vagus develop or should the individual be abnormally vagosensitive,[6] the correct combination of E factor and vagus overactivity should promote the development of auricular fibrillation.

In hypertension, vagal overactivity is probably a constant reflex phenomenon increasing in vagosensitive patients. When heart failure with auricular distention and venous engorgement occurs, the stretch of the auricle may contribute the necessary stimulus (E) which, when in association with vagus overactivity, precipitates auricular fibrillation. It thus becomes clear why this irregularity is so often associated with heart failure, being rightly regarded as an important evidence of the existence of heart failure.

SUMMARY

Acetyl-β-methylcholine chloride converted the normal cardiac mechanism of four hyperthyroid patients and ten electrically stimulated cats into auricular fibrillation. In a patient with auricular flutter and 2:1 block the same substance converted the flutter into auricular fibrillation with a very slow ventricular rate. Auricular flutter did not appear in passing to or from fibrillation. The drug also altered the ventricular complex producing Q and S waves as well as displacements of the ST segments.

CONCLUSIONS

1. Auricular fibrillation is produced by the interaction of two factors on the auricular myocardium: (*a*) preponderant vagus activity and (*b*) an E factor such as thyroxine, electric shock or possibly simple auricular distention.

2. Acetyl-β-methylcholine chloride can rapidly convert auricular flutter into fibrillation and is thus a valuable agent for speedy slowing of the ventricular rate.[11]

333 Cedar Street.

7. Lewis, Thomas: The Mechanism and Graphic Registration of the Heart Beat, London, Shaw & Sons, 1925.

8. Evans, C. L.: The Physiology of Plain Muscle, Physiol. Rev. **6:** 358-398 (April) 1926.

9. Legendre, R.: Action de l'étirement et de la striction sur les fibres nerveuses, Compt. rend. Soc. de biol. **88:** 352-355 (Feb.) 1922.

10. de la Chapelle, C. E.; Graef, Irving, and Rottino, Antonio: Studies in Rheumatic Heart Disease, Am. Heart J. **10:** 62-78 (Oct.) 1934.

11. Dr. W. F. Verdi gave permission to use his private patients in these studies; Dr. W. Cohen took the electrocardiograms of the clinical experiments, and Merck and Company, Rahway, N. J., furnished ample supplies of acetyl-β-methylcholine chloride (Mecholin).

From the Departments of Gynecology and Pathology of the Mount Sinai Hospital.

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EVALUATION OF THE CONSTITUTIONAL EFFECTS OF LARGE DOSES OF ESTROGENIC PRINCIPLE

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The present study was undertaken in an attempt to answer some of the questions propounded by the Council on Pharmacy and Chemistry of the American Medical Association in a recent report on the estrogenic substance theelin.[1] Without dwelling at length on the merits or demerits of the substance as a therapeutic agent, the report of the Council pertinently states: "Evidence of deleterious effect from the clinical administration of estrogenic substance is not conclusive, but the possibility deserves serious consideration, particularly if the large doses more recently employed clinically should come into common usage." This study attempts to delineate the constitutional effects of huge doses of one of the estrogenic substances on the human female, as reflected in the ordinary laboratory and clinical studies at our disposal. This work is correlated with histologic studies of the vital organs of animals subjected to injections of enormous doses of the substance over periods varying from seven to fifty-seven days.

In the clinical study reported here, only hydroxyestrin benzoate in oil was employed; in the experimental

investigations on animals, dihydroxyestrin and, occasionally, theelin were injected. The three products were tested in our laboratory by the Allen-Doisy method and were found to contain the number of rat units herein indicated:

Hydroxyestrin benzoate,[2] 10,000 rat units per cubic centimeter.

Dihydroxyestrin, 5,000 rat units per tablet (the tablets were dissolved in oil before injection).

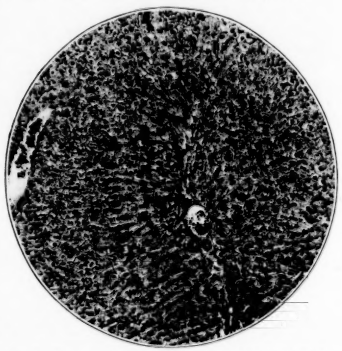

Fig. 1.—Section of rabbit liver before injection of dihydroxyestrin (from a photomicrograph with a magnification of 85 diameters).

Theelin in oil, 200 rat units (labeled 1,000 international units) per cubic centimeter.

The clinical survey is limited to a group of twenty-nine adult women and one pubertal girl. These thirty patients, an integral part of a larger group treated with estrogenic substance, were sufficiently cooperative to permit completion of the studies. The indications for the administration of the estrogenic principle included amenorrhea, hypomenorrhea, dysmenorrhea, kraurosis vulvae, and the menopausal syndrome. An evaluation of the efficacy of estrogenic substances in the treatment of such disorders is not within the scope of the present discussion and is reserved for a forthcoming report, which will deal with the indications, dosage and limitations of estrogenic substance therapy. We may, however, state at this juncture that the severe menopausal syndrome and kraurosis vulvae are the two conditions requiring the use of the maximum doses employed in the treatment of these patients. The clinical observations and laboratory procedures were performed, in each instance, before and after the administration of estrogenic substance. The data recorded include body weight, blood pressure, basal metabolic rate, effect on the normal menstrual rhythm, complete blood chemistry (including sugar, urea nitrogen, uric acid, creatinine, cholesterol, calcium and chlorides), bleeding and coagulation times, urinalysis and complete blood counts (including differential study of leukocytes). In some instances, data of minor importance were not available for analysis because of the patient's lack of cooperation. Thus, the hemoglobin values were completed (before and after treatment) in twenty-nine patients, whereas the leukocyte and differential counts were available for computation in only twenty-seven patients. The omitted data appear as blank spaces in the tables.

The dose of estrogenic substance administered varied with the indication and the individual's response to the therapy. The substance was given intramuscularly in every instance at intervals of four days. Fifteen of the thirty patients received 10,000 rat units per dose throughout the entire period of observation. The remaining number were given initially several doses of 10,000 rat units and subsequent doses of 5,000 or 2,000 rat units, depending on the patients' responses to the treatment. The total amount of estrogenic substance given to each patient was as follows: 260,000 rat units to one; 200,000 rat units to ten; 150,000 rat units to fifteen, and somewhat less than 100,000 rat units to only four. The period of treatment averaged three months. Only two patients were treated for six months.

No ill effects, either constitutional or local, were noted other than an occasional instance of local irritation. The latter was probably caused by failure to inject the oily solution intramuscularly.

EFFECT ON BASAL METABOLISM

The basal metabolism rate of twenty-two patients was recorded before and after administration of estrogenic substance. Only one, a well woman free of symptoms other than primary amenorrhea, showed a significant change; namely, a fall from plus 26 per cent to minus 9 per cent. Since the patient manifested no hyperthyroid symptoms and since the fall in metabolic rate was to a figure within normal limits, no special significance may be attached to the change. It is noteworthy that another patient with a pretreatment rate of minus 30 per cent showed a final figure of minus 36 per cent. It seems that the administration of large doses of estrogenic substance has no demonstrable effect on the basal exchange.

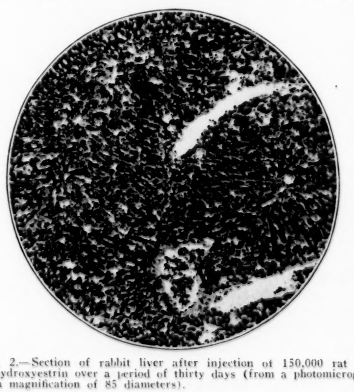

Fig. 2.—Section of rabbit liver after injection of 150,000 rat units of dihydroxyestrin over a period of thirty days (from a photomicrograph with a magnification of 85 diameters).

EFFECT ON BODY WEIGHT

The body weight of each patient was observed at frequent intervals. No significant change was noted in the entire series. This is in accord with the observation of Kaufmann.[3] The constancy of body weight during

2. We are indebted to Drs. Gregory Stragnell and Erwin Schwenk of the Schering Corporation for the generous supply of progynon-B (hydroxyestrin benzoate) and the dihydroxyestrin employed in the clinical and major part of the experimental work.

3. Kaufmann, C.: Die Behandlung der Amenorrhöe mit hohen Dosen der Ovarialhormone, Klin. Wchnschr. **12**: 1557 (Oct. 7) 1933.

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prolonged administration of estrogenic substance was also noted in animals by Leiby [4] and in our experimental work.

EFFECT ON BLOOD PRESSURE

Twenty-six had normal blood pressures prior to the period of administration of estrogenic substance; three had systolic pressures of 140 mm. of mercury, and one (patient 10), who had nephritis with hypertension, had an initial blood pressure of 170 systolic, 100 diastolic.

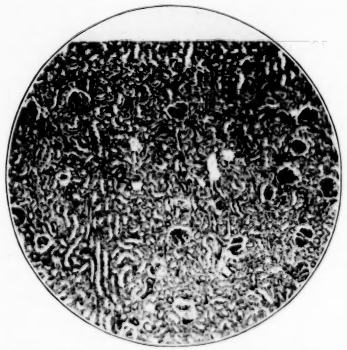

Fig. 3.—Section of rabbit kidney before injection of dihydroxyestrin (from a photomicrograph with a magnification of 85 diameters).

No significant change occurred in the blood pressures of the twenty-six normal and the three slightly hypertensive women. Our clinical observation is in accord with the experimental studies of Laqueur [5] and Melchionna,[6] who found no blood pressure changes in animals after the administration of estrogenic substances. Liebhart,[7] however, recently reported a moderate fall in the blood pressures of normal pubertal and mature females treated with relatively small doses of the hormone. The hypertension of our patient with nephritis remained unaffected throughout the period of treatment. This is in accord with the observation of Ayman,[8] who failed to reduce arteriolar hypertension with moderate doses of estrogenic substance. We are at present treating by means of large doses of the substance a small group of women with essential hypertension and are, thus far, unable to corroborate the successful results of Fellner [9] and Mayrhofer.[10]

EFFECT ON COMPLETE BLOOD COUNT

The hemoglobin estimations (Sahli) and the erythrocyte counts showed no unusual changes following the use of estrogenic substance. In twenty-nine patients, the hemoglobin values remained within normal limits; anemia did not appear in any of them. The apparent relief of a marked secondary anemia in case 11 (table 1), during the administration of large amounts of the estrogenic substance, was probably the result of simultaneous administration of iron, arsenic and phosphorus. The erythrocyte counts remained constant and within normal limits. Our results concur with those of Hirst,[11a] who administered estrogenic substances of varying amounts to new-born infants.

We found no appreciable change in the leukocyte counts of the twenty-seven patients following estrogenic substance treatment. Those patients who, prior to treatment, had a slight leukocytosis (cases 7 and 22, table 1) showed approximately the same count at the termination of the injections. The differential counts were likewise practically unchanged in the group of twenty-seven. In his series of new-born infants, Hirst[11a] found a relative decrease in polymorphonuclear leukocytes, a moderate rise in lymphocytes, and a tendency to eosinophilia after theelin administration. Ten of our patients did show an insignificant decrease in polymorphonuclear leukocytes and a corresponding rise in lymphocytes; six, on the other hand, showed exactly the reverse change; the remaining eleven patients presented no variation from the control counts. It is therefore illogical to ascribe any changes in the relative percentages of polymorphonuclear leukocytes and lymphocytes to the administration of estrogenic substances. The variations are within normal limits. A slight tendency to eosinophilia was, however, noted in three patients who had normal eosinophil values at the beginning of treatment and 4, 5 and 6 per cent, respectively, at the termination of the course of injections. Furthermore, eleven of the twenty-seven patients who had no eosinophils prior to administration of estrogenic substances showed normal percentages (1 to 3 per cent) following treatment.

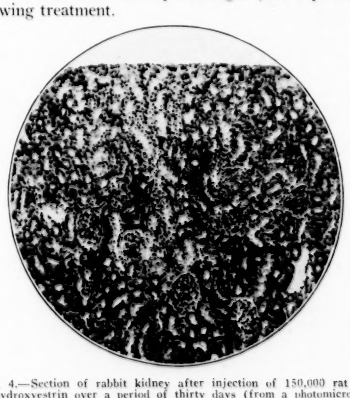

Fig. 4.—Section of rabbit kidney after injection of 150,000 rat units of dihydroxyestrin over a period of thirty days (from a photomicrograph with a magnification of 85 diameters).

EFFECT ON BLEEDING AND COAGULATION TIMES

As shown in table 1, there were no deviations from normal in the bleeding times of the twenty-three patients examined. Thirteen of the twenty-four patients whose coagulation times were studied showed no variations from the normal, either before or after treatment.

4. Leiby, G. M.: The Effect of Theelol on the Weights of Pituitary, Adrenal and Thyroid, Proc. Soc. Exper. Biol. & Med. **31:** 15 (Oct.) 1933.

5. Laqueur, E.: Ueber weibliches Sexualhormon, im bes. das Menformon, Klin. Wchnschr. **6:** 390 (Feb. 26) 1927.

6. Melchionna, Robert: The Effect of Theelol on the Blood Pressure, Heart Rate, and Respiratory Rate, J. Biol. Chem. **91:** 653 (May) 1931.

7. Liebhart, S.: Ueber den Einfluss des Ovarialhormons auf den Blutdruck, Zentralbl. f. Gynäk. **58:** 1896 (Aug. 11) 1934.

8. Ayman, David: The Treatment of Arteriolar Hypertension with Crystalline Ovarian Hormone (Theelin), Am. J. M. Sc. **187:** 806 (June) 1934.

9. Fellner, O. O.: Hormonale Behandlung der Arteriosklerose (Hypertonie), Med. Klin. **29:** 1713 (Dec. 15) 1933.

10. Mayrhofer, H.: Menformon in der Therapie der essentiellen Hypertonie, Wien. klin. Wchnschr. **47:** 232 (Feb. 23) 1934.

11. Hirst, J. C.: (*a*) Further Observations on the Effect of Female Sex Hormone upon the Blood of New-Borns, Am. J. Obst. & Gynec. **28:** 431 (Sept.) 1934; (*b*) The Influence of Female Sex Hormone upon Blood Coagulation of the New-Born, ibid. **26:** 217 (Aug.) 1933.

Nine of this group, who had shown a tendency to prolonged blood coagulability (from seven to nine minutes) prior to treatment with estrogenic substance, showed a moderate reduction (from one to three minutes) at the close of the treatment period. Hirst [11b] found that the aqueous solution of progynon, unlike theelin, increases the coagulation time of new-born infants. The fact is

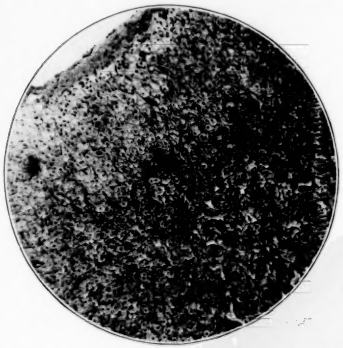

Fig. 5.—Section of rabbit adrenal before injection of dihydroxyestrin (from a photomicrograph with a magnification of 85 diameters).

that the aqueous solution of the estrus-inducing hormone, dispensed under the name of progynon, is a mixture of theelin and theelol and therefore should not differ in its effect on coagulation time from that of theelin.

One may conclude that healthy adult females show no significant change either in coagulation or in bleeding time with massive doses of estrogenic substance. The reduction observed in the coagulation time in the nine patients who showed somewhat high values prior to treatment is in accord with the observations of Hirst [11b] on new-born infants. He states: "Abnormally long coagulation and bleeding times, as well as spontaneous bleeding other than vaginal, were corrected by injections of theelin." By inference one may assume that the hormone has some beneficial influence on the course of hemophilia—an effect attributed to the estrogenic substance by Birch.[12]

EFFECT ON BLOOD CHEMISTRY

Following the administration of estrogenic substance, no striking variations were noted in the chemical constituents of the blood, as measured by the ordinary laboratory means (table 2). The values were unchanged whether or not the initial study showed very high or very low figures.

The unchanged serum calcium determinations concur with those of Dixon,[13] Frei and Emmerson [14] and others in blood studies on animals. The constancy of the cholesterol values is of unusual interest in view of the close chemical relationship between the estrus-inducing hormone and cholesterol. In case 28 a low cholesterol content changed to a normal level following the treatment; in case 19 the reverse occurred (table 2). No importance need be attached to these fluctuations, since neither of the patients showed any evidence of thyroid dysfunction.

Though the blood sugar levels of normal women remain unaffected with the use of large doses of the estrogenic substance, the blood and urine of diabetic women show an appreciable decrease in the sugar content during injections of the product. This observation is limited to only three patients, two of whom received 400 rat units of the estrogenic substance daily and one of whom received 10,000 rat units every fourth day for a period of from four to six weeks. The maximum fall in blood sugar observed in these three diabetic patients was 60 mg. There was, in each instance, a return to the former level soon after withdrawal of the treatment. This clinical observation is in accord with observations of Barnes [15] on the blood sugar levels of pancreatectomized dogs injected daily with 200 rat units of amniotin (one of the commercial products of the estrogenic hormone). Theoretically, the fall in blood sugar of the experimental animal following injections of the estrogenic substance is caused by inhibition of the diabetogenic function of the anterior pituitary lobe, since hypophysectomy in the pancreatectomized dog produces the same results.

EFFECT ON KIDNEY FUNCTION (URINALYSIS)

Repeated examinations revealed no albumin or casts in the urines of the twenty-nine normal women. Nor did we find any increase in the number of casts and quantity of albumin in the urine of the one nephritic patient (number 10) as a result of the administration of 120,000 rat units of the estrogenic principle given over a period of five weeks. The finer tests for kidney function other than blood chemistry determinations were not performed.

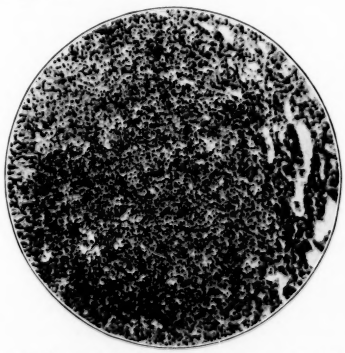

Fig. 6.—Section of rabbit adrenal after injection of 150,000 rat units of dihydroxyestrin over a period of thirty days (from a photomicrograph with a magnification of 85 diameters).

EFFECT ON MENSTRUAL RHYTHM

The effects produced by estrogenic substances on abnormal types of menstruation is not within the scope of this report. They will be considered in detail at a later date. However, the effect of the hormone on the regular menstrual cycle is germane to the subject under discussion. We noted the menstrual cycles of seventeen

12. Birch, C. L.: Hemophilia and the Female Sex Hormone: Preliminary Report, J. A. M. A. **97**: 244 (July 25) 1931.

13. Dixon, T. F.: The Influence of Ovarian and Anterior Pituitary Hormones on Calcium Metabolism, Biochem. J. **27**: 410, 1933.

14. Frei, W., and Emmerson, M. A.: Der Serumkalkspiegel beim Rinde mit besonderer Berücksichtigung der Beziehungen zum Geschlechtsapparat, Biochem. Ztschr. **226**: 355, 1930.

15. Barnes, B. O.; Regan, J. F., and Nelson, W. O.: Improvement in Experimental Diabetes Following the Administration of Amniotin, J. A. M. A. **101**: 926 (Sept. 16) 1933.

regularly menstruating women treated with the large doses of estrogenic substance because of hypomenorrhea, dysmenorrhea, adenosis of the breasts, and the like. Only five of the seventeen are included in the present series of thirty patients (cases 4, 5, 6, 15 and 16 in tables 1 and 2).

reported intermenstrual staining of from one to two days' duration while receiving treatment. All of the six patients who showed disturbed menstrual rhythm as a result of the treatment with estrogenic substance continued to menstruate regularly during a follow-up period of nearly a year.

TABLE 1.—*Blood Studies Before and After Intensive Administration of Estrogenic Substance*

	Bleeding Time, Minutes		Coagulation Time, Minutes		Hemoglobin (Sahli)		Erythrocytes, Millions		Leukocyte Count		Differential Leukocytes: Polymorphonuclear Leukocytes		Small Lymphocytes		Large Lymphocytes		Eosinophils		Basophils		Transitionals	
Case	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
1	2.0	1.5	7.5	5.0	85	91	4.1	4.7	7,150	7,050	55	46	44	50	1	..	..	2	..	2	..	..
2	1.5	1.5	7.0	6.0	95	95	5.1	5.0	7,450	7,700	72	67	24	28	1	..	2	1	..	..	1	3
3	2.0	2.0	6.5	6.5	89	86	4.5	4.3	9,700	8,050	57	48	39	46	1	4	..	..	1	..	2	2
4	1.5	1.5	5.0	4.5	85	87	4.5	4.7	6,550	7,150	67	61	30	34	..	3	2	1	1	..	..	1
5	...	...	...	...	88	90	...	...	...	...	..	..	..	..	..	..	..	..	..	..	..	..
6	1.5	1.5	7.0	6.5	92	91	4.9	4.9	9,000	8,500	68	69	28	28	..	..	2	6	..	..	1	1
7	2.0	2.0	7.0	6.5	84	85	4.4	4.5	12,250	13,100	72	74	28	24	..	..	..	2	..	..	..	..
8	2.0	1.0	5.0	4.0	94	92	5.1	4.9	7,400	8,250	56	56	44	34	..	1	..	..	..	..	..	1
9	1.5	1.5	6.0	5.0	87	88	4.7	4.4	8,000	7,000	63	58	36	39	..	2	1	1	..	..	..	..
10	...	...	...	...	81	90	4.2	4.5	8,400	8,850	73	60	25	1	2	35	..	..	..	..	..	..
11	...	...	4.5	4.0	78	74	3.4	3.8	7,400	8,800	..	..	..	..	..	..	..	..	..	..	..	..
12	2.5	2.0	8.0	5.0	85	87	4.0	4.4	8,000	7,100	72	66	26	27	..	2	2	4	..	..	..	1
13	2.5	2.5	5.0	5.0	96	93	5.2	5.0	9,150	8,750	58	59	36	33	1	4	4	3	1	..	..	1
14	1.5	1.5	5.0	4.5	88	87	4.3	4.2	7,000	7,050	75	58	23	38	..	3	..	1	..	..	2	..
15	2.0	2.5	6.0	6.0	78	72	4.8	4.9	10,300	7,500	55	71	40	27	4	1	1	..	..	..	..	1
16	3.5	3.0	9.0	8.5	81	83	4.2	4.0	7,500	7,950	56	55	42	24	1	5	1	5	..	..	..	1
17	(Studies not completed)																					
18	3.5	3.0	6.0	6.0	80	84	4.2	4.3	7,100	6,550	50	55	41	40	6	4	..	..	2	..	1	1
19	2.0	2.5	7.5	8.0	86	86	4.3	4.3	9,200	8,200	68	64	31	24	..	12	..	..	..	..	1	..
20	1.5	2.0	7.5	6.5	83	84	4.2	4.2	6,800	7,950	56	70	39	..	2	24	..	3	..	2	..	1
21	2.0	2.5	8.0	7.0	83	92	4.3	5.0	8,350	8,150	66	70	33	26	..	1	..	2	1	1	..	..
22	....	....	....	....	80	92	4.4	4.7	14,900	10,500	83	83	13	30	3	6	..	..	..	1	1	..
23	2.0	2.0	6.0	5.5	82	83	3.9	4.0	9,150	8,750	76	69	24	28	..	2	..	1	..	..	..	..
24	1.5	2.5	6.5	8.0	91	94	4.8	5.0	7,000	7,250	63	60	30	35	1	2	4	2	2	1	..	..
25	2.0	2.0	9.0	5.5	78	80	3.6	3.8	9,900	8,350	68	60	27	34	1	4	..	2	..	..	4	..
26	2.0	2.5	5.5	9.0	84	82	4.2	4.4	9,150	8,550	63	62	28	34	2	4	5	..	2	..	..	..
27	1.5	1.5	3.0	4.0	87	83	4.7	4.3	9,850	8,450	56	53	42	45	2	1	..	1	..	..	..	..
28	...	...	...	...	84	84	....	....	....	....	..	..	..	..	..	..	..	..	..	..	..	..
29	3.5	3.0	6.0	6.0	80	84	4.2	4.3	7,100	6,550	50	55	41	40	6	4	..	..	1	1	2	..
30	...	...	...	...	80	78	4.0	4.0	7,800	8,000	..	..	..	..	..	..	..	..	..	..	..	..

TABLE 2.—*Blood Chemistry Studies Before and After Intensive Administration of Estrogenic Substance*

	Sugar		Urea Nitrogen		Creatinine		Cholesterol		Uric Acid		Chlorides		Calcium	
Case	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
1	97	99	15.6	11.3	1.25	1.42	141	139	4.22	4.16	495	500	11.68	10.51
2	101.5	100	14.8	22.1	1.12	1.27	156	222	4.74	4.80	475	465	12.88	9.30
3	113	102	10.0	13.3	1.32	1.41	176	198	3.14	3.28	490	495	.....	.....
4	119	110	9.2	8.6	1.32	1.64	184	203	3.88	3.32	490	493	8.37	10.42
5	111	114	13.8	15.2	....	....	152	168	3.26	3.34	....	....	.....	.....
6	120	118	11.5	11.2	1.40	1.51	160	187	2.86	2.72	495	479	.....	.....
7	122	97	11.4	8.7	1.12	1.22	153	137	2.86	2.96	505	480	9.30	10.24
8	...	...	12.2	13.1	1.39	1.47	....	....	2.70	3.42	....	....	.....	.....
9	79.5	98	11.1	12.2	1.00	1.41	....	....	3.50	3.18	....	....	.....	.....
10	90	96	....	....	....	....	....	....	....	....	....	....	9.00	8.79
11	81	89.5	13.2	13.9	....	....	....	....	2.60	3.00	....	....	.....	.....
12	...	...	15.6	18.3	1.53	1.62	188	147	3.66	2.34	480	485	.....	.....
13	132	110	7.8	9.8	1.42	1.07	....	....	5.72	5.22	473	470	10.60	11.02
14	120	94	13.1	13.4	1.33	1.29	173	160	3.84	3.26	480	503	10.47	8.65
15	87	87	10.0	9.0	....	....	....	....	4.20	3.00	504	532	9.50	10.10
16	74.5	99	11.1	10.3	1.00	1.82	....	....	3.50	2.82	....	....	.....	.....
17	90	92	15.9	15.8	....	....	....	....	....	....	....	....	.....	.....
18	107	94	15.6	15.7	1.24	1.29	163	173	2.66	3.02	521	493	10.92	10.14
19	100	96	13.0	10.2	1.20	1.19	160	123	3.00	3.78	....	....	.....	.....
20	116	99	13.7	10.4	1.16	1.33	168	203	3.44	3.52	518	500	9.56	10.23
21	107	87	11.4	14.7	1.43	1.26	153	153	3.18	3.64	495	490	9.77	10.12
22	133	145	12.3	10.9	1.88	1.27	186	206	3.76	3.32	574	478	.....	.....
23	102	88	12.7	14.4	1.16	1.29	159	147	3.22	4.12	463	483	.....	.....
24	...	...	10.6	11.0	....	....	....	....	....	....	....	....	.....	.....
25	111	94	10.4	15.3	1.18	1.53	192	181	3.04	2.88	490	506	.....	.....
26	117	109	18.5	17.6	1.46	1.33	181	192	3.12	3.38	485	480	9.52	10.43
27	92	92	10.1	11.4	1.27	1.18	208	236	2.80	2.58	475	500	.....	.....
28	120	102	12.2	15.5	1.27	1.29	122	163	4.00	4.16	495	505	.....	.....
29	107	94	15.6	15.7	1.24	1.29	163	173	2.66	3.02	521	493	10.92	10.14
30	95	105	12.0	14.0	....	....	....	....	....	....	....	....	.....	.....

Eleven of the seventeen patients showed no changes in the menstrual rhythm either during or after administration of estrogenic substance. Six patients experienced a single delay in the appearance of the menstrual flow, varying from one to three weeks, during the course of three months' treatment with large doses of estrogenic substance. Four of these six patients, as well as one of the eleven who had no disturbed rhythm,

Illustrative of the nature of the temporary disturbance in menstrual rhythm is the protocol of one of the patients, shown in table 3. The establishment of a new date of onset of the subsequent menses following a short delay in the flow in six of the group may, in the light of present limited knowledge of sex physiology, be attributed to a temporary inhibition of the gonad-stimulating function of the anterior pituitary lobe,

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which the estrogenic hormone is known to produce in the experimental animal (Leonard and his associates,[16] Moore and Price [17] and others).

The deleterious effects of large doses of estrogenic substances on the human ovary are conjectural. The presence of a high content of estrogenic substance of the blood during pregnancy militates against this possibility. Experimentally, Allen [18] and Katzman [19] have shown that the pituitary inhibition resulting from the administration of estrogenic substance is only slightly reflected on the ovarian structures of adult rodents, unless huge amounts are administered. Hohlweg,[20] for instance, maintains that daily injections of 100 rat units of crystalline dihydroxyestrin over a period of thirty days stimulate hyperluteinization in adult rats. Be that as it may, it seems that large doses do disturb the menstrual rhythm of regularly menstruating women, at least temporarily.

The effect of intensive treatment with estrogenic substances on the fertility of the human female is difficult to ascertain from a study of a small group of patients. Most of our seventeen regularly menstruating women are sterile for various reasons. None have as yet conceived. One of Clauberg's [21] patients conceived shortly after the administration of 400,000 mouse units (80,000 rat units) of estrogenic substance. Two of our sterile patients (not included in this study) conceived shortly after the administration of 22,000 and 18,000 rat units, respectively. Experimentally, Katzman [19] found no reduction in fertility of adult rats following the administration of relatively large amounts of estrogenic substance.

TABLE 3.—*Nature of the Delay and the Establishment of a New Date of Onset of the Menstrual Flow Incident to Intensive Administration of Estrogenic Substance*

White woman, aged 26	
Menarche at 14 years, regular 31-day cycle	
Chief complaint: dysmenorrhea	
Menses: January 1	
February 2	
←——February 10	Hormone treatment
March 5	
April 18 (delay of 16 days)	
May 19	
←——June 1	
June 20	
July 21	

EFFECT ON NORMAL BREASTS

Only a few of the group of women treated showed evident growth of the mammary glands. This phenomenon is more marked in some children who are treated with relatively large doses of estrogenic substances for gonorrheal vaginitis. The growth is temporary, receding rapidly after withdrawal of the substance.

EFFECT ON LIBIDO

Absence of libido is more often caused by psychic factors and abnormal marital relationships than by deficiencies of the estrus-inducing factor. In this type of patient, one would not expect any increase in libido from treatment with estrogenic substance. That an increase of libido does occur in castrated women during treatment with estrogenic substance was reported by Werner and Collier [22] and was likewise observed by some of our patients. The pathologic increase in libido following estrogenic substance therapy, as postulated by Poate,[23] is, we believe, restricted to the small group of patients who already have a high estrogenic content of the blood. We have found this to be true by repeated blood hormone titrations in three highly neurotic women suffering from nymphomania.

EXPERIMENTAL OBSERVATIONS

As a corollary to our clinical studies, we subjected thirty immature and adult rabbits to daily injections of enormous doses of the estrogenic substance over periods varying from seven to fifty-seven days. They received, individually, total amounts varying from 80,000 to 150,000 rat units—quantities relatively far in excess to those given our patients. Nevertheless, none of the vital organs (liver, kidneys, heart, lungs and adrenal bodies) showed either macroscopic or microscopic evidence of pathologic changes, as shown in the photomicrographs. Description of the changes in the pituitary gland, breasts, ovaries, fallopian tubes and uterus will be given in another communication dealing mainly with the endocrine response of the experimental animal to such large doses. We may state at present, however, that the response of the endocrine glands (stimulative or regressive) varies with the age of the animal, the dose, the length of the treatment and, above all, the species susceptibility of the animal to the estrogenic substance.

Experimental observations cannot, therefore, be translated accurately into human equations. We must await further clinical reports of a reliable nature before we render an opinion on the nature of endocrine response of the human being to large doses of the estrogenic substance. From a careful survey of our clinical material, only part of which is herein reported, we are inclined to believe that doses within the limits mentioned are harmless after the child-bearing age and in younger women who no longer desire offspring.

SUMMARY

From a survey of the literature and the clinical study of thirty patients, it was found that injections of from 100,000 to 200,000 rat units of estrogenic substance, given in divided doses over periods of from two to three months, produce no appreciable changes in body weight, basal metabolism, blood pressure, blood count, coagulation and bleeding times, blood chemistry and urine.

In six of seventeen regularly menstruating women, injections of these large quantities of estrogenic substance produced a temporary delay in the menstrual flow (from one to three weeks) and established in these six patients a new date of onset of the menses. This phenomenon is apparently due to a temporary inhibition of the anterior pituitary lobe which normally controls ovarian function. The effect on fertility is, as yet, unknown.

Growth of the mammary glands and increased libido were observed in a few of the treated patients.

16. Leonard, S. L.; Meyer, R. K., and Hisaw, F. L.: The Effect of Estrin on Development of the Ovary in Immature Female Rats, Endocrinology **15**: 17 (Jan.-Feb.) 1931.
17. Moore, C. R., and Price, Dorothy: Gonad Hormone Functions, and the Reciprocal Influence Between Gonads and Hypophysis with Its Bearing on the Problem of the Sex Hormone Antagonism, Am. J. Anat. **50**: 13 (March) 1932.
18. Allen, Edgar: Sex and Internal Secretions, Baltimore, Williams & Wilkins Company, 1932, p. 392.
19. Katzman, P. A.: A Note on the Effect of Theelin, Theelol and the Luteinizing Substance on Reproduction, Proc. Soc. Exper. Biol. & Med. **29**: 700 (March) 1932.
20. Hohlweg, W.: Veränderungen des Hypophysenvorderlappens und des Ovariums nach Behandlung mit grossen Dosen von Follikelhormon, Klin. Wchnschr. **13**: 92 (Jan. 20) 1934.
21. Clauberg, C.: Studien an infantilen und insuffizienten menschlichen Uteri (Zum Problem der Ovarialinsuffizienz), Ztschr. f. Geburtsh. u. Gynäk. **107**: 331, 1934.
22. Werner, A. A., and Collier, W. D.: The Effect of Theelin Injections on the Castrated Woman, with Histologic Report, J. A. M. A. **100**: 633 (March 4) 1933.
23. Poate, E. M.: Theelin, letter to editor, J. A. M. A. **100**: 1792 (June 3) 1933.

Relatively larger doses of the estrogenic substance (from 80,000 to 150,000 rat units) than those employed clinically produced neither macroscopic nor microscopic changes in the vital organs of thirty rabbits. The response of the ovaries to huge doses of the estrogenic substance is either degenerative or stimulative, depending on the species and age of the test animals and the duration of administration of the substance.

1829 Pine Street.

HEART DISEASE IN THE CHICAGO AREA

A STUDY OF THE ETIOLOGIC FACTORS IN ONE THOUSAND CASES

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CHICAGO

Since the publication of the Criteria for the Classification and Diagnosis of Heart Disease,[1] sponsored by the American Heart Association, and the pioneer work of White[2] and Wyckoff,[3] increased interest has been manifested in studying the etiologic factors operative in the production of heart disease. Authorities are agreed that the incidence of heart disease is increasing each year. Perhaps the pertinent point in stemming this increase may be elucidated through an examination of the causative factors.

The value of the work of the committee that has advocated the publication of the Criteria for the Classification and Diagnosis of Heart Disease in directing current thought toward the consideration of heart disease from the etiologic, anatomic and physiologic points of view is becoming more and more obvious. The standards set forth by this committee merit adoption by all hospitals and cardiologists, thus permitting uniform reports of the incidence and type of heart disease throughout the United States. The Middle West was negligent in reporting any statistical data until Flaxman's report[4] appeared from the Cook County Hospital.

We here present our studies of 1,000 consecutive cases of heart disease encountered in private and consultation practice in the Chicago area. Both hospital and office patients are included, although the majority were ambulatory. With three exceptions, they were all of the white race; two were Negroes and one was Japanese. All ages are included, but adults preponderate over children.

A problem that confronts an author in presenting such material statistically is the frequency of more than one etiologic factor in the same individual. For example, a patient may have both hypertensive vascular disease and syphilis. The pulmonary heart (cor pulmonale) case may also show hypertension, arteriosclerosis or syphilis. Thyrotoxicosis may be complicated by rheumatic infection or hypertension. A number of complicating problems of this sort might be cited.

In some of the statistical reports of the etiologic factors of heart disease, the percentages are computed by counting the total number of etiologic factors and then calculating the percentage of any given factor from this sum rather than from the total number of patients. It is our belief that this method gives somewhat an incorrect concept of the actual facts. We have been unable to devise any absolutely satisfactory method of presenting our data which takes into consideration the multiplicity of etiologic factors in single cases and still presents a true picture of the percentage basis from the total number of cases involved. Our final conclusion on this problem was to consider twelve main groups, as follows:

1. Rheumatic infection.
2. Hypertension.
3. Arteriosclerosis.
4. Syphilis.
5. Thyroid disease.
6. Pulmonary diseases.
7. Congenital causes.
8. Neurologic causes.
9. Toxic causes.
10. Traumatic causes.
11. Bacterial entities.
12. Unknown or unclassified causes.

Our material will be presented under these twelve headings and subclassification made in each of these groups to demonstrate the interrelationship of the various factors.

Chart 1 is a diagrammatic representation of the number of cases in each general group. The shaded area of each block represents the number of cases complicated by secondary etiologic factors. The distribution of these secondary complications is further discussed under the separate headings. Rheumatic infection, hypertension and arteriosclerosis are overwhelmingly in preponderance. Syphilis, thyrotoxicosis and pulmonary disease are next in frequency. Bacterial, congenital, toxic and traumatic factors rank least. Functional heart disease was encountered in eighty cases, or 8 per cent, of the total. Eighty-four cases were unclassified or the etiologic factor was unknown.

RHEUMATIC HEART DISEASE

The criteria for the establishment of rheumatic heart disease were those described in the Criteria for the Classification and Diagnosis of Heart Disease,[1] which are as follows:

1. History of polyarthritis, chorea, muscle or joint pains, of subcutaneous nodules, and evidences of a characteristic structural lesion of the heart.
2. Evidence of a characteristic structural lesion plus a history of periods of recurrent fever and cardiac insufficiency.
3. Evidence of carditis of the type associated with active rheumatic heart disease even in the absence of other rheumatic manifestations.

Rheumatic heart disease was present in 292 cases. Of these, 22.2 per cent, or sixty-five cases, were complicated by secondary factors, as demonstrated in chart 2. Occasionally there were as many as three etiologic factors present in a single case.

The most common complicating factor was thyrotoxicosis, occurring in 9.5 per cent, or twenty-eight

1. Criteria for Classification and Diagnosis of Heart Disease: New York Tuberculosis and Health Association, eds. 1, 2 and 3, 1928, 1929, 1931.
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3. Wyckoff, John, and Lingg, Claire: Etiology in Organic Heart Disease, Am. Heart J. **1**: 446 (April) 1925.
4. Flaxman, Nathan: Heart Disease in the Middle West, Am. J. M. Sc. **188**: 639 (Nov. 21) 1934.

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cases. This association is worthy of more than passing comment. Although goiter and hyperthyroidism are common in this area, this statistical figure does not represent an accurate picture of this relationship. Many of these cases of valvular disease were examined only on one occasion, and only a few were followed through the entire rheumatic heart cycle from the inception of the infection and the cardiac involvement to death. Undoubtedly a greater number than 9.5 per cent would have been complicated by thyrotoxicosis had longer observation been possible. Even with the incidence of 1 to 9.5, the examiner must be ever watchful not to overlook a hyperthyroidism masked by a valvular lesion or the converse. This combination was considered worthy of a case report by Cabot,[5] who remarked a single occurrence of rheumatic heart disease and thyrotoxicosis in his experience. The low incidence of thyrotoxic disease in Cabot's area explains the infrequency. It is of interest to note that Parry's [6] original case report of exophthalmic goiter was complicated by rheumatic infection. Graves [7] also reported the combination, and Trousseau [8] in 1835 wrote at some length on the subject.

Comparison of our figures as to the frequency of rheumatic heart disease (29.2 per cent) with the figures of other observers is of interest. Flaxman [4] has recently reported his study made in the Cook County Hospital, Chicago, reporting a frequency of 16.7 per cent, much lower than ours. His estimate is made from hospital entries on indigent patients with a higher age average. White [9] reports an incidence of 39.5 per cent in the New England area. In the Pacific Northwest, Coffen [10] reports the incidence of 0.1 per cent for rheumatic fever. Viko [11] recorded a frequency of 44 per cent in the Rocky Mountain region. Wyckoff and Lingg [3] gave an incidence of 42.7 per cent in the New York area. Stone and Vanzant [12] indicate 7.3 per

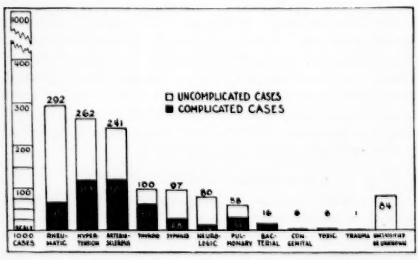

Chart 1.—Demonstration of relative frequency of individual etiologic factors.

cent in Texas. Glazer [13] from an autopsy study reported only 3 per cent in Cincinnati. These variations represent geographic or climatic influence on the occurrence of rheumatic infection, assuming that all the patients included in the series acquired infection in the area studied. In this respect, Nichol [14] reported 413 cases with an incidence of 25 per cent rheumatic heart disease in his practice in Florida, but only in six of these cases did the rheumatism develop in the Southern area. It has been well established, however, that rheumatic infection is higher on the Atlantic seacoast and less in the South and Southwest.[15] Our figure of 29.2 per cent

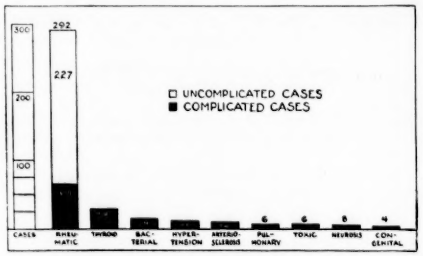

Chart 2.—Demonstration of the combination of rheumatic infection with other etiologic factors.

would place the incidence of rheumatic heart disease in the Chicago area lower than the Eastern seacoast or the Rocky Mountain region but much higher than the Cincinnati figure (3 per cent) of Glazer, or the incidence of the South.

The rheumatic group showed a ratio of seven females to five males, approximately that reported by many authors of almost equal distribution among the sexes. The age incidence was not at variance with other reports that the majority of rheumatic heart disease occurs in youth or early adult life.

The frequency of involvement of other viscera by infectious processes is worthy of mention. The association of acute rheumatic fever, chorea and tonsillitis with rheumatic heart disease is not a new subject. In those patients under observation for a period of years, we have found that pneumonitis, pleuritis and colitis were unusually frequent. Clinically and by roentgen examination, evidence of active pleuritic or pneumonic pathologic changes may occasionally be found. Chronic infection of the pelvic viscera and biliary tract was encountered in females. The relationship of infections in other viscera to the cardiac infection warrants further careful study.

Rothschild, Kugel and Gross,[16] who studied 161 cases of rheumatic heart disease at autopsy, found that "106 showed active infection of the heart," which is in accord with our clinical studies of activity.

5. Cabot Case Records: Coexistence of Thyrotoxicosis and Rheumatic Heart Disease, New England J. Med. **201**: 1056 (Nov.) 1929.
6. Parry, C. H.: Collections from the Unpublished Writings of the Late Caleb H. Parry, M.D., London.
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8. Trousseau, A.: Trousseau's Clinical Medicine, New Sydenham Society, 1868.
9. White, P. D., and Jones, T. D.: Am. Heart J. **3**: 302 (Feb.) 1928.
10. Coffen, T. H.: Am. Heart J. **5**: 99 (Oct.) 1929.
11. Viko, L. E.: Am. Heart J. **6**: 264 (Dec.) 1930.
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15. Coburn, A. F.: The Factor of Infection in the Rheumatic State, Baltimore, Williams and Wilkins Company, 1931. Faulkner, J. M., and White, P. D.: The Incidence of Rheumatic Fever and Rheumatic Heart Disease, J. A. M. A. **83**: 425 (Aug. 9) 1924. Harrison, T. R., and Levine, S. A.: Notes on the Regional Distribution of Rheumatic Fever and Rheumatic Heart Disease in the United States, South. M. J. **17**: 914 (Dec.) 1924. Seegal, David, and Seegal, Beatrice C.: Studies in the Epidemiology of Rheumatic Fever, J. A. M. A. **89**: 11 (July 2) 1927. Paul, J. R.: Epidemiology of Rheumatic Fever, a Preliminary Report with Special Reference to Environmental Factors in Rheumatic Heart Disease and Recommendations for Future Investigations, Am. Heart Assn., 1930, Metropolitan Life Ins. Co. Press, New York.
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HYPERTENSION

The criteria for the diagnosis of heart disease due to hypertension as given in the Criteria for the Classification and Diagnosis of Heart Disease are as follows: "Persistent hypertension associated with enlargement of the heart." The frequent association of arteriosclerosis is discussed. In this study these standards were followed. The most difficult problem was to arrive at a reasonably accurate decision concerning the significance of associated arteriosclerosis. In general, we have added arteriosclerosis as an associated factor in patients in whom there was a well marked peripheral arteriosclerosis or who presented clinical evidence of coronary, retinal or cerebral arteriosclerosis. There is no doubt that our figures are inaccurate in this respect. Decision has been a personal estimate of degree. If one were to follow all the hypertensive cases from beginning to end, the frequency of an associated arteriosclerosis would undoubtedly be much higher.

Two hundred and sixty-two patients were classified in the hypertensive vascular group, representing an incidence of 26.2 per cent of the total. Chart 3 is a diagram showing the comparative frequency of the other etiologic factors associated with hypertension. One third, or eighty-nine cases, were classified as having an associated arteriosclerosis. Almost one tenth, or twenty-five cases, were thyrotoxic. Eleven cases were also classified in the rheumatic group. Nine of our cases were classified as having pulmonary disease. We are inclined to believe that this figure is too low. In our early records, there is no doubt that we paid too little attention to pulmonary factors, and it is our impression that pulmonary disease is much more often a complicating factor in this group than our figures would indicate. There were only four cases in which syphilis was associated.

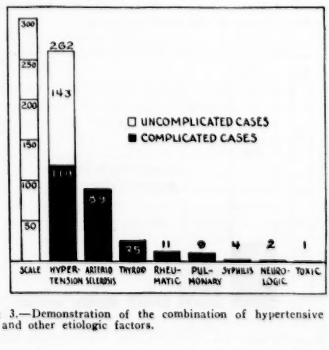

Chart 3.—Demonstration of the combination of hypertensive vascular disease and other etiologic factors.

Comparison may be made of our figures with those of Flaxman, who records an incidence of hypertension of 43 per cent in his studies to our figure of 26.2 per cent. Again the difference is due to the material studied and to the fact that the indigent hospital group contained 28 per cent of the Negro race. The incidence in New England, as reported by White,[9] was 29.2 per cent. The incidence of hypertension in other statistical reports appears to be greatest in the South, where figures range from 47 per cent to 68 per cent,[12] and least in the Rocky Mountain region, where Viko [11] reported only 14.9 per cent.

In view of the fact that the majority of our patients are in the age group of 40 years or above, systemic disease of many types has been frequently tabulated as a complication in the study of this hypertensive vascular group. The nephritic cases have been included in this group when associated with hypertension.

In studying our older records, it appears that insufficient attention has been paid to urologic disease. The

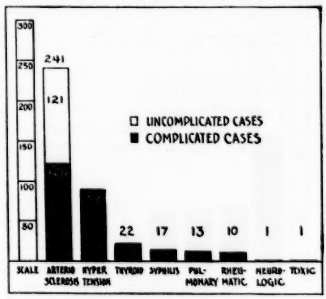

Chart 4.—Demonstration of arteriosclerotic heart disease and other etiologic factors.

urologic pathologic condition has been brought to our attention in cases that have been under observation for some years and in which acute problems have developed, such as cystitis, renal colic, hematuria or pyuria. In the male, asymptomatic prostatism, old stricture and chronic urethral and prostatic infection were readily overlooked. In the female, bladder deformities, pyelitis and hydronephrosis were overshadowed by more obvious cardiac symptomatology. The relationship to the hypertensive vascular problem has not always been clear. Obstruction with infection in the urinary tract, however, was seriously detrimental to the welfare of the hypertensive and arteriosclerotic cardiac patient. Diabetes mellitus was another common complication. Biliary tract disease was also frequently found.

ARTERIOSCLEROTIC HEART DISEASE

Cases were classified under arteriosclerotic heart disease when there was evidence of generalized arteriosclerosis, coronary arteriosclerosis, aortic sclerosis (nonsyphilitic), pulmonary arteriosclerosis, or fibrosis of the myocardium as defined by the Criteria for Classification and Diagnosis.

Two hundred and forty-one patients, or 24.1 per cent of the total, were listed under this heading. The secondary etiologic factors are presented diagrammatically in chart 4. Hypertensive vascular disease was found to be the most common complicating factor, occurring in eighty-nine cases, or 36.9 per cent of the 241 cases.

There were twenty-two patients with thyrotoxicosis and coronary sclerosis. They were all over 40 years of age. Syphilis was represented by only seventeen cases. There were only ten cases of rheumatic infection in this combination. These were patients in whom the rheumatic infection had apparently entirely healed and had been quiescent for years. The frequent association of other diseases, as mentioned in the hypertensive group, also applied to the arteriosclerotic patients.

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THYROID HEART DISEASE

Heart disease of thyroid etiology as listed by the Criteria is as follows:

Criteria for Diagnosis of Thyroid Heart Disease due to Adenoma with Hyperthyroidism or Exophthalmic Goiter:

1. Evidence of hyperthyroidism and enlargement of the heart.
2. Evidence of hyperthyroidism associated with abnormal cardiac function such as paroxysmal or permanent auricular fibrillation.

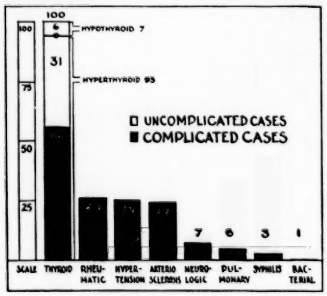

Chart 5.—Thyroid group.

Criteria of Heart Disease Due to Myxedema:

1. Evidence of hypothyroidism with enlargement of the heart, with or without cardiac insufficiency.
2. Favorable response to the administration of thyroid extract.

One hundred cases, or 10 per cent of the series, were classified in this group, of which ninety-three were hyperthyroid and seven were hypothyroid. In the hypothyroid cases, six were uncomplicated by any other known etiologic factor and one was complicated by hypertension and urologic disease. The group of thyrotoxic patients was the most interesting of the series, in that sixty-two cases (66.6 per cent) were complicated by organic or structural heart disease and, in addition to this, seven cases were complicated by neurocirculatory asthenia as presented diagrammatically in chart 5.

TABLE 1.—*Incidence in Hyperthyroid and Main Group*

	Hyperthyroid Group (93 Cases)	Main Group (1,000 Cases)
Rheumatic	30.1%	29.2%
Hypertension	26.8%	26.2%
Arteriosclerosis	23.8%	24.1%
Neurologic	7.5%	8.0%
Syphilis	3.2%	9.7%
Pulmonary	5.3%	5.8%
Bacterial	1.0%	1.0%

The common complicating factors in this group were rheumatic disease, hypertension and arteriosclerosis. The other etiologic factors, except congenital, toxic and trauma, were also encountered. Comparison of the incidence of these secondary factors with the incidence of the same factors in the main group show them to be similar (table 1).

The effect of thyrotoxicosis on the welfare of the structurally damaged heart was of great importance as to operative risk, prognosis and postoperative morbidity. The thyrotoxicosis exaggerated the primary cardiac problem, and thyroidectomy relieved this burden. In those cases in which there were no other etiologic factors than thyrotoxicosis, in which thyroidectomy was performed; the cardiac situation was no longer a clinical issue, except in a few cases of recurrence of thyrotoxicosis.

In the Criteria for Classification and Diagnosis,[1] "evidence of hyperthyroidism, associated with abnormal cardiac function such as paroxysmal or permanent auricular fibrillation" is listed as a basis for the diagnosis of hyperthyroidism. In our studies, auricular fibrillation, either paroxysmal or permanent, has been found only in the presence of other obvious factors and structural lesions, commonly rheumatic valvular disease, hypertensive vascular disease, coronary arteriosclerosis and myocardial fibrosis. It has been our impression that the primary basis for the occurrence of auricular fibrillation was the structural lesion and the thyroid toxemia the secondary exciting factor. In this small series the arrhythmia was not encountered in uncomplicated thyrotoxicosis. We are making a further search to clarify this issue in a larger series of thyrotoxic patients, and also to study frequency of structural pathologic changes.

Comparison of our statistics and other reports shows great variation. Flaxman's[4] report from the Cook County Hospital lists an incidence of 2.6 per cent. In the New England area reported by Cabot[17] and White and his associates[18] the incidence is from zero to 2.9 per cent. In the West and Northwest, Coffen[10] and Viko[11] report incidences of 6.1 per cent and 9.3 per cent respectively. The high incidence of goiter in the Great Lakes area and northwestern United States is commonly accepted.

SYPHILITIC GROUP

The Criteria for Classification and Diagnosis of Syphilitic Heart Disease are as follows:

1. History of syphilitic infection and evidence of a characteristic structural lesion of the heart or aorta.

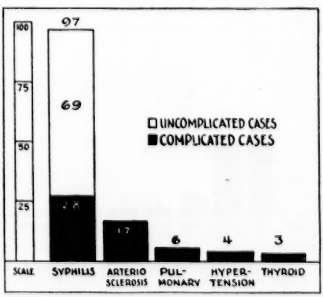

Chart 6.—Demonstration of the combination of syphilitic heart disease and other etiologic factors.

2. A characteristic structural lesion of the heart or aorta without a history of syphilis but with a positive Wassermann reaction.
3. A characteristic structural lesion of the heart or aorta together with evidences of syphilitic disease, elsewhere, such as cerebrospinal syphilis, even in the absence of a positive Wassermann reaction or a history of syphilitic infection.

17. Cabot, R. C.: The Four Common Types of Heart Disease, J. A. M. A. **63**: 1461 (Oct. 24) 1914.
18. White and Myers.[9] White and Jones.[9] White, P. D.: Heart Disease, New York, Macmillan Company, 1932.

We have followed these criteria with two exceptions: We have encountered two cases of syphilitic pulmonary arteritis with a cor pulmonale, one of which was proved at autopsy. There was no autopsy in the second case, but it was equally definite clinically.

Ninety-seven cases were classified under this heading and twenty-eight cases, or 28.8 per cent, were complicated by secondary factors, as demonstrated in

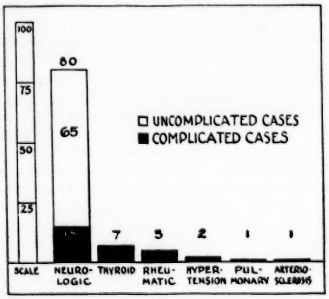

Chart 7.—Neurologic group.

chart 6. Only four cases of hypertension were encountered in this group, while in a similar study of indigent patients the combination of syphilis and hypertension was much more common.

Other authors report incidences of syphilitic heart disease as from 1.1 per cent to 21.4 per cent. That syphilis has been overlooked in some cases is probably true. The number of patients in this group was too small to calculate reliable figures as to age, sex and other factors.

NEUROLOGIC

The Criteria for Classification and Diagnosis gives the following:

Criteria for Diagnosis of Cardiac Psychoneurosis:

1. Presence of definite psychoneurosis in the history or examination of the patient.

2. Presence of the symptoms and signs mentioned without structural cardiac disease being present or without its being present in sufficient degree to account for the symptoms.

Reflex Action. Certain patients may be subject to physiological disturbances of the heart action as a result of reflexes arising in other parts of the body, and especially in the abdominal viscera. Premature contractions, paroxysmal tachycardia, and sinus arrhythmia are the most frequent disturbances of such origin.

We have considered the psychoneurotic group and the reflex group together in this study. Eighty patients were classified in this category. In fifteen cases, or 18.7 per cent, an organic lesion complicated the syndrome of neurocirculatory asthenia. These complicating factors are presented in chart 7.

Thyrotoxicosis was listed in seven cases. Six of these patients came under our observation after thyroidectomy. An effort was made to determine whether the thyrotoxicosis had been an error of diagnosis or whether the two entities may occur in the same individual. These patients had been examined by numerous physicians and consultants with varied opinions. It was impossible to render a decision. We had the opportunity of studying our patient before and after thyroidectomy. We failed to discern the functional syndrome of neurocirculatory asthenia prior to operation.

In this group there were five cases of rheumatic heart disease, two of hypertension and one of pulmonary and arteriosclerotic disease.

PULMONARY HEART DISEASE

Criteria for Diagnosis of Heart Disease due to Pulmonary Emphysema:

1. The presence of pulmonary emphysema.
2. Evidences of cardiac insufficiency with more than usual cyanosis.
3. Evidences of enlargement of the right ventricle.

Only fifty-eight cases, or 5.8 per cent, were classified in this group; of them forty-one cases (70.6 per cent) were associated with other etiologic factors, as presented in chart 8, showing their frequency. We are inclined to believe that we have overlooked the pulmonary factor more often than any other.

TABLE 2.—*Types of Pulmonary Disorders in this Series*

Condition	Cases
Bronchiectasis	25
Asthma and bronchitis	13
Tuberculosis	8
Syphilis	6
Hodgkin's disease	2
Deformity of the spine and thorax	2
Unknown	2
Metastatic cancer of lung	1
Actinomycosis	1

The following types of pulmonary pathologic conditions were encountered in this series as shown in table 2:

In one case of hay fever congestive heart failure developed in the second trimester of pregnancy. One patient in this group died with coronary thrombosis, and autopsy revealed a cor pulmonale. The only cause demonstrated for the emphysema and the increased size

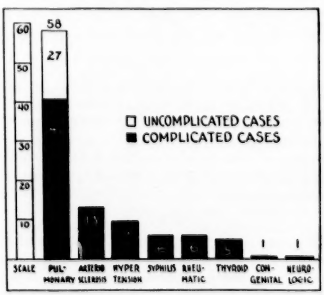

Chart 8.—Demonstration of the combination of pulmonary heart disease and other etiologic factors.

of the right ventricle was a history of continuous athletic training over a period of twenty-two years. A well marked pulmonary arteriosclerosis was also found.

Evidence of enlargement of the right ventricle was seldom of value in establishing this diagnosis unless the patient was under observation for more than a year, with two roentgenograms for comparison. Right axis deviation in the electrocardiogram was observed as a development in the later stage of the disease.

BACTERIAL GROUP

The criteria for the diagnosis of Bacterial Endocarditis are listed as follows:

Evidence of cardiac valvular disease or of a congenital abnormality associated with

1. Signs of sepsis.
2. Positive blood culture.
3. Embolic phenomena.

Sixteen cases, or 1.6 per cent, were classified in this group, all due to Streptococcus viridans.

All of these were complicated by either rheumatic (fourteen cases) or congenital disease (two cases).

One case was of unusual interest because of the combination of subacute bacterial endocarditis and a severe thyrotoxicosis.

CONGENITAL GROUP

Congenital entities listed in the Criteria include: Anomalies of position of the heart or great vessels, coarctation of the aorta, patent ductus arteriosus, pulmonic stenosis, patency of the septum and congenital defect of the pericardium.

Only six cases were encountered, five of which were complicated by other etiologic factors. In four cases a superimposed rheumatic valvulitis developed, in two cases subacute bacterial endocarditis, in two toxic factors and in one case a deformity of the thorax.

TOXIC GROUP

The Criteria as listed for the toxic group are as follows:

Evidence of a definite toxin (bacterial, mineral, vegetable) associated with

1. Structural lesion of the heart.
2. Abnormal cardiac function.

Twelve cases, or 1.2 per cent, were included in this group. Seven of the cases were due to diphtheritic infection and five were secondary to pneumonia. Secondary etiologic factors were present in eight cases; rheumatic infection, six cases; congenital disease, two cases; arteriosclerosis, one case; and hypertension, one case.

TRAUMATIC GROUP

"Trauma. Structural cardiac lesions occur as the result of penetrating wounds, severe blow upon the chest or crushing injuries." This again is quoted from the Criteria.

One case of this type is included in the series of a traumatic pericarditis as a result of a severe crushing injury of the thorax.

COMMENT

While a study of this type is of value in determining the relative frequency of the various types of cardiac disease in a given geographic area and allows comparison with other areas, we were impressed that it fails to convey a correct impression of many of the practical issues in the course of a cardiac case.

A majority of the minor factors are neglected in presentation of these data. Respiratory infections, dietary factors, pregnancy, emotional crises, overexertion, surgical procedures, anesthesia effects, and many other factors cannot be included or correctly evaluated.

The combination of two or more etiologic factors in one patient presents an interesting field of study. In this series 31.6 per cent, or 316 cases of the 1,000, were in this group, with multiple etiologic factors. Again it is necessary to point out the inadequacy of statistical studies to portray accurately such relationships. To have an exact analysis of this problem one should include cases that are under observation over the entire clinical course of the heart problem.

In the rheumatic heart group, for example, only 22.2 per cent are complicated by secondary etiologic factors. If this entire group had been studied over the complete rheumatic heart cycle, undoubtedly a greater number would be found to have been complicated by hypertension, arteriosclerosis, goiter or syphilis. Only fourteen cases were complicated with subacute bacterial endocarditis, or 4.7 per cent. White [18] quotes an incidence of 4 per cent. Karsner and Bayless [19] in their studies of coronary arteries in rheumatic disease report that "rheumatic fever regularly produces disease of the coronary arteries." Only ten cases, or 2.9 per cent, in our series were classified in the arteriosclerotic group.

Lisa and Chandlee [20] reported a study of six cases of the combination of syphilis and rheumatic infection. In one case the rôle of syphilis equaled that of the rheumatic infection, while in five cases the rheumatic infection preponderated. In this series we never encountered this combination. In our studies in the Cook County Hospital, however, it is of frequent occurrence clinically, and usually in Negro patients, as the foregoing observers indicate. However, we have never been able to prove conclusively the identity of the two lesions anatomically.

The combination of syphilis and hypertension occurred in only three patients, and syphilis and arteriosclerosis occurred in fifteen cases. Horine and Weiss [21] studied the relationship of syphilis and hypertension and reported that "syphilis had no etiologic bearing on essential hypertension." This again is a combination frequent in the Negro race and in the indigent patient and much less common in private cases.

In completing this survey, we have been impressed with the value of classifying our patients into etiologic groups. Our attention has been better directed toward treatment of the causative factors with better therapeutic results. Prognosis has been simplified.

While many cases of cardiac disease may be readily classified in the major groups of rheumatic, hypertensive or arteriosclerotic heart disease, there are no doubt frequent errors. The factor of error is reduced in those patients under observation for long periods of time. The history taken from the patient has been a factor of prime importance, as well as the physical examination. One cannot underestimate the necessity of the fluoroscopic, roentgen and electrocardiographic studies.

Lastly, one cannot fail to learn that each cardiac patient presents a highly individual problem, with one or more essential causative factors and many minor issues affecting his clinical course.

180 North Michigan Avenue.

19. Karsner, H. T., and Bayless, Frances: Coronary Arteries in Rheumatic Fever, Am. Heart J. **9**: 557-581 (June) 1934.
20. Lisa, J. R., and Chandlee, Gertrude J.: The Heart and Great Vessels in Combined Syphilitic and Rheumatic Infection, Arch. Int. Med. **54**: 952 (Dec.) 1934.
21. Horine, E. F., and Weiss, M. M.: Relationship of Syphilis to Hypertension, Am. Heart J. **6**: 121 (Oct.) 1930.

Economy in Buying Food.—The better the economy with which food is purchased, the better the chance that the diet will contain all that contributes to positive health.—Sherman, H. C.: Food and Health, New York, Macmillan Company, 1934.

Clinical Notes, Suggestions and New Instruments

ACUTE EXACERBATION OF LATENT GONORRHEAL URETHRITIS AFTER FIFTY YEARS FOLLOWING PROSTATECTOMY

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WOLFEBORO, N. H.

It is deemed of interest to report this case, since careful search of the literature reveals no similar ones. Many authors, in general discussion, mention that gonococcic infection may recur following operations but mention no specific instances. Dr. A. L. Wolbarst[1] says: "It is a curious but explainable fact that a long-forgotten gonococcal infection may be revived and an acute inflammation develop as the result of an injury, inflammation, or a surgical operation in some distant part of the body." Similar general statements are the only type that are found in the literature.

REPORT OF CASE

History.—T. D. H., a white man, aged 70, retired from business, admitted to the Huggins Hospital, Oct. 12, 1934, complained chiefly of complete inability to void for the preceding twelve hours. For the past year, gradually increasing in severity to date, he had noticed dysuria, nocturia, frequency and feebleness of the stream of urine along with diminished, unrelieving amounts being passed at a single micturition.

The past history was essentially irrelevant except for a definite acute attack of gonorrheal urethritis followed by a course of metal urethral sounds fifty years previously. This attack was apparently successfully treated, and there had been no urethral discharge or other genito-urinary symptoms since that time. The patient later became married and there are now two grown, mature children as a result of this union. The wife and children are and have been quite healthy in every respect.

Examination.—Physical examination revealed but few senile changes consistent with a relatively rugged man of his age whose only complaint was inability to void.

Rectal examination showed a diffuse and symmetrical enlargement of the prostate, the palpated surface being smooth and firm. Gram's stains of prostatic smears revealed from two to five leukocytes per high power field but no organisms.

There was no urethral discharge, nor could any be expressed by manual manipulation. The easy passage of a number 18 French soft rubber catheter through the urethra to the bladder evidenced the absence of any urethral strictures.

Laboratory examination on admission revealed: red blood cells, 3,580,000; hemoglobin, 60 per cent; white blood cells, 13,900, with 80 per cent polymorphonuclear leukocytes. Several Kahn tests of the blood were negative. Blood nonprotein nitrogen was 60 mg. per hundred cubic centimeters, subsequently 43 mg. prior to the second stage of the operation. Urine showed a trace of albumin, many pus cells and a few red blood cells, all of which cleared under suprapubic drainage.

A first stage suprapubic cystotomy was done, October 26, and on November 14 the second stage of the suprapubic prostatectomy was carried out. A pathologic report gave a diagnosis of benign diffuse hypertrophy of the prostate.

Clinical Course.—The patient had a generally normal postoperative course, abetted by a whole blood transfusion at the end of the second week. A creamy, purulent penile discharge was noted for the first time, December 3, about three weeks after the second stage prostatectomy. Many smears were made of this urethral pus by different, competent individuals on separate days, such smears being stained by Gram's method and examined microscopically. An abundance of Gram-negative intracellular diplococci typical of gonococci were found on each occasion. This discharge persisted until about three weeks after voluntary micturition through the urethra had been established; thereafter no pus could ever be seen or expressed from the meatus.

Subsequent urologic examination showed the presence of several areas of stricture in the posterior urethra, presumably due to the gonorrheal urethritis, which required the use of sounds for dilation. The passage of sounds, however, did not stir up any further urethral discharge or symptomatic burning, and the urine has been free from albumin and pus since three weeks after the healing of the suprapubic wound and the disappearance of the urethral pus.

SUMMARY

There are no reports in the literature of exacerbation of latent gonorrheal urethritis following prostatectomy.

This patient had a definite gonorrheal urethritis at the age of 20 years. This was successfully treated without sequelae. The patient married and became the father of two normal, healthy children, and his wife never had any symptoms or signs of gonorrhea. The patient himself had no signs of urethritis from the time of the first, apparently successfully treated, attack until a suprapubic prostatectomy was done fifty years later.

Prostatectomy apparently caused an acute exacerbation of the gonorrheal urethritis. Three weeks afterward, typical gonorrheal pus with gonococci seen on repeated Gram's stains of the smears taken of the pus were noted. This discharge persisted for about three weeks after urine was passed through the urethra for the first time since operation and has not been seen since. Subsequent strictures of the posterior urethra, presumably due to this last attack of gonorrheal urethritis, necessitated the use of metal sounds for dilation.

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SPONTANEOUS RUPTURE OF COLD ABSCESS OF CHEST WALL: REPORT OF A CASE

ALLEN S. JOHNSON, SPRINGFIELD, MASS.

The following case of spontaneous rupture of a cold abscess of the chest wall with drainage of a pleural effusion is reported because of the apparent rarity of the phenomenon. Meade[1] says in regard to a tuberculous abscess of the soft parts of the chest wall that "whether it starts in the pleura or other deep seated layer the process always advances outward, either directly or after a lateral deviation. Practically all writers agree that inward spread is unknown." In the case herewith reported, however, this abscess developed spontaneously, not in a needle tract after aspiration, and ruptured both inward and outward, thereby replacing the pleural effusion with a pneumothorax. The studies of Leggett[2] and Emerson[3] indicate that such a sequence of events is most unusual in the case of a pleural effusion not secondarily infected, and I can find no report of such a phenomenon in an extensive search through the literature on this subject.

G. M., a man, aged 49, a clerk, seen by another physician five weeks before admission to the hospital complained of cough and dyspnea. The patient's father had had tuberculosis, and two uncles had died of the disease. The patient himself had always been susceptible to respiratory infections, which were often accompanied by dry pleurisy. He frequently had a temperature and often had drenching night sweats. He had had a productive cough, attributed to smoking, since early adult life and had had mild hemoptyses on several occasions. It was difficult to date the onset of the present illness, but the dyspnea had been growing progressively worse for several weeks. The significant physical signs at this time were those of a right-sided pleural effusion. Roentgenograms showed the right lung to be almost entirely collapsed by fluid, extending up to the third interspace anteriorly; above this was air, which further collapsed the lung. This suggested that the effusion had

From the Huggins Hospital.

1. Wolbarst, A. L.: Gonococcal Infection in the Male, St. Louis, C. V. Mosby Company, 1930, p. 34.

1. Meade, R. H., Jr.: Localized Tuberculosis of the Chest Wall, Ann. Surg. **97**: 247 (Feb.) 1933.
2. Leggett, E. A.; Myers, J. A., and Levine, I.: Spontaneous Pneumothorax, Am. Rev. Tuberc. **29**: 348-361 (March) 1934.
3. Emerson, in Tice, Frederick: Practice of Medicine, Hagerstown, Md., W. F. Prior Company, Inc. **5**: 610, 1921.

occurred as a sequel to a spontaneous pneumothorax but a careful history yielded no evidence of such a sequence of events. The left upper lobe showed extensive tuberculous infiltration, and there was some mediastinal shift to the left.

The patient was then admitted to the local tuberculosis hospital. The sputum was loaded with tubercle bacilli on all occasions. Blood counts were not remarkable. Blood Hinton and Wassermann tests were negative. The sedimentation rate (Cooper's method) was a fast normal (70 per cent in one hour). A diagnostic chest tap posteriorly ten days after admission revealed slightly cloudy straw colored fluid. A smear showed no organisms or pus cells and culture yielded no growth.

The patient's course during the next two months was not remarkable. He ran an irregular temperature up to 100.6 F., a pulse of 100 and respirations of 25. A reddish, brawny, itching area of induration about 6 cm. in diameter then developed in the seventh interspace in the right nipple line. During the next few days this became definitely painful and fluctuant. In order to rule out rib involvement by x-ray, 3,000 cc. of pleural fluid was aspirated posteriorly. Even this large amount failed to lower the fluid level below the abscess, but the danger of an abrupt shift of the mediastinum contraindicated further aspiration at this time. The fluid removed was cloudy and straw colored with a specific gravity of 1.020 and showed numerous white blood cells. No tubercle bacilli or other organisms were found in smears, and culture on ordinary mediums yielded no growth. The patient was having very little systemic reaction from the abscess and only slight local pain, so that evacuation of the abscess was not imperative. While we were waiting for the return of our x-ray technician, however, the abscess ruptured spontaneously, about three weeks after it was first noticed. Such pus as may have been evacuated was obscured by the enormous quantity of yellow watery fluid, which poured through the sinus from the pleural cavity so that cultures were not obtainable before contamination had occurred. Apparently what had appeared to be a superficial abscess gradually working its way toward the surface had ruptured inward and outward at the same time. Roentgenograms now showed the pleural effusion to have been completely drained and replaced by a pneumothorax, which was maintaining the lung and mediastinum in the same relative positions. The ribs did not appear to be involved. During the development of this abscess and after its rupture the patient's temperature, pulse and respirations remained about the same; but he volunteered the information that he now felt much better and had a better appetite than he had had for months.

A few days after the rupture of the abscess, daily irrigations of the sinus tract were instituted with azochloramide, 1:3,300. These were well tolerated by the patient and cultures from the sinus and by aspiration through pipets introduced into the pleural cavity showed no growth a month after rupture of the abscess. The overgrowth of granulation tissue in the sinus then began to interfere with adequate irrigation of the cavity and secondary infection developed. The clear serous discharge became purulent and the patient began to lose the weight which he had gained during the preceding two months. A month of daily irrigation with gentian violet was of no evident benefit, and the azochloramid irrigations were resumed. Six weeks of this treatment have materially lessened the amount of the discharge, though it is still purulent. The patient feels much better, however, and his renewed appetite has resulted in his regaining all the weight that had been lost. The roentgenogram is almost identical with that taken after the rupture of the abscess four and one-half months ago. He is still afebrile and is allowed bathroom privileges. The only change in the sinus is the loss of 4 square centimeters of integument about the opening with the production of a shallow, indolent ulcer, which has gradually increased in size in spite of ultraviolet irradiation and various local applications.[4]

121 Chestnut Street.

4. A supply of azochloramid for the treatment in this case was furnished by Dr. Elliott Weyer of Wallace and Tiernan, the manufacturers, Belleville, N. J.

Special Article

GLANDULAR PHYSIOLOGY AND THERAPY

THE INTERNAL SECRETION OF THE PANCREAS

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NOTE.—*This article and the articles in the previous issues of* THE JOURNAL *are part of a series published under the auspices of the Council on Pharmacy and Chemistry. Other articles will appear in succeeding issues. When completed, the series will be published in book form.*—ED.

The time-honored and productive physiologic methods of studying the function of an organ are (1) to remove it completely or in part and to observe the abnormal effects attributable to its absence, and (2) to make extracts of the tissue in various ways and to study the mechanism of action of the fractions that are found to possess specific physiologic potency. The pancreas has lent itself admirably to this procedure in the case of both internal and external secretions. Since this article is, in large part, a preface to a consideration of the therapeutics of pancreatic preparations, the space available will be devoted to a consideration of the internal secretion.

REMOVAL OF THE PANCREAS

When the pancreas is completely removed from a dog (and the effects in the other mammals that have been studied are similar), a characteristic syndrome rapidly develops.[1] When a diet including all the known essentials is provided, the animals may live indefinitely if adequate amounts of insulin are administered. The diets used have included preparations containing the pancreatic enzymes and a source of choline (or of related substances with similar effects), which apparently is necessary to prevent deposition of excessive amounts of fat in the livers of these animals. The dogs recover rapidly from the depancreatization and appear normal, but the diabetic state quickly supervenes when insulin is discontinued. The sugar content of the blood begins to rise within a very short time, the length of which depends on the size of the last dose of insulin, and increases from the normal level of from 0.08-0.11 per cent to 0.20-0.40 per cent or higher within twenty-four hours. The urine gives a positive Benedict qualitative test for sugar when the blood sugar rises above approximately 0.16 per cent. This point, the so-called renal threshold, is the level of blood sugar above which large amounts of sugar are excreted in the urine. In some animals the "threshold" rises when the diabetic state is allowed to persist. (There are minute amounts of dextrose and some other sugars in normal urine.) The excretion of nitrogen is increased, and this may be taken to indicate protein breakdown, but some doubt exists as to the accuracy of the conventional calculation; i. e., protein-urinary nitrogen × 6.25, particularly when this is applied in short-term experiments. The amount of dextrose formed from protein in the diabetic subject has been calculated from the increased dextrose output when protein is given to the phlorhizinized dog.

From the Department of Physiology and the School of Hygiene, University of Toronto.

1. von Mering, Joseph, and Minkowski, O.: Diabetes mellitus nach Pankreasextirpation, Arch. f. exper. Path. u. Pharmakol. **26**: 371 (Jan.) 1889.

It is very doubtful whether phlorhizin poisoning and pancreatic diabetes are comparable conditions, but studies of the former suggest that the amino acids glycine, alanine, cystine, aspartic and glutamic acid yield dextrose but that others, such as tyrosine, leucine and phenylalanine, do not yield dextrose but increase the excretion of ketone bodies. The ratio of dextrose to nitrogen excreted in phlorhizin poisoning is 3.6:1, but this ratio is rarely observed in depancreatized dogs and indeed that obtained is so variable that in most circumstances little significance can be attached to it. The ratio is low under certain conditions in animals on a high protein diet, and there is evidence that the addition of small amounts of fat may increase it somewhat. The question of sugar formation from fatty acids will be briefly discussed later. It is established that glycerol may be converted to sugar, so some extra sugar excretion may be expected when glycerides, i. e., neutral fats, are administered. (Glycerides are reported not to increase the sugar excretion of a phlorhizinized animal.) In the fasting diabetic subject the blood sugar and sugar excretion are maintained at high levels. The sugar is apparently formed from body protein largely in the liver, since the blood sugar of the diabetic subject falls rapidly after hepatectomy. The loss of protein contributes to the rapid decrease in body weight observed in depancreatized animals.

The disturbed metabolism of fat in the depancreatized animal is indicated by the accumulation of the ketone bodies in the blood and by the excretion of excessive amounts in the urine. The ketosis in a fat dog is greater than in a lean one, but this species is characterized by its efficiency in metabolizing fats without ketosis. The loss of body fat is rapid, but the ketosis may be so severe even in this species that the animal dies of coma before the fat reserves are depleted.

Beta-oxybutyric acid is a relatively nontoxic product. It can be estimated by oxidizing to acetone and determining the amount of the latter substance. Aceto-acetic acid, on the other hand, is more toxic probably because of its enolic form $CH_3COH-CH.COOH$. It is stated that this substance stimulates the respiratory center and depresses the higher centers of the brain, causing in these ways "air hunger" and the dimmed perception and loss of consciousness of diabetic coma. The evidence does not justify the conclusion that aceto-acetic acid is the sole cause of this syndrome. Aceto-acetic acid is decomposed in the bladder and lungs, and acetone and carbon dioxide are formed. Acetone, $CH_3—C:O—CH_3$, is excreted in the urine and expired air. Aceto-acetic acid in blood may be converted by mild hydrolysis to acetone and the latter can be estimated by various procedures.

The neutral fat content of the blood increases, owing probably to the augmented rate of mobilization of depôt fat, and there is also a rise in cholesterol esters and phospholipids. Since there are small amounts of the ketone bodies present in normal blood, it is preferable to consider these substances as intermediary products in the oxidation of fatty acids. When the rate of breakdown of the acids is excessive, as in pancreatic diabetes, these ketone bodies accumulate in the blood.

A little space may be given here to the two closely related questions (1) the formation of sugar from fatty acids in the depancreatized animal, and (2) whether pancreatic diabetes is characterized by an overproduction of sugar, an underutilization of sugar or both. With regard to the first, it is well established that this transformation takes place in plants, and there is considerable indirect evidence that may be interpreted as favoring this possibility in animals; but direct proof of the change is conspicuous by its absence. It is difficult to prove that the change cannot take place, and failures to obtain evidence in favor of it may be due to the method of investigation. In spite of the attention this question has attracted, it must be left in this unsatisfactory state. A final answer would do much to clarify the field.

If overproduction of dextrose were the only abnormality in diabetes, fat as well as protein would be required to furnish material. Very few authorities will deny that the evidence for the increased rate of production of sugar from protein in pancreatic diabetes is satisfactory. While there is, in my opinion, an abundance of evidence that the depancreatized dog can still burn sugar—all the criteria of sugar combustion in the normal have been satisfied—it is not permissible to conclude that there is no interference with this process. Convincing experimental evidence for deficient utilization of dextrose in diabetic heart muscle was at one time thought to be available, but it now appears that the chief fuel of heart muscle is lactic acid, which is taken up from the blood, and not dextrose. The amount of sugar utilized by a hepatectomized dog is apparently definitely less when the pancreas also is removed. The rapid sugar utilization in the hepatectomized diabetic animal and the production of a diabetic condition by the administration of the diabetogenic substance of the anterior pituitary, which apparently acts by stimulating the liver to produce more dextrose, tend to emphasize overproduction rather than underutilization. It is preferable to consider, however, that both mechanisms play a part in the production of the diabetic condition and to concentrate attention on the development of quantitative methods by which accurately to determine the extent of the overproduction or underutilization.

Studies of isolated muscles appeared to indicate that carbohydrate alone is burned, but there are now many facts which suggest that other food materials are used. While the possibility exists that these may be converted to sugar in the muscle before use, it is much simpler and more in accord with the evidence to consider that fat and protein as well as sugar may be used directly.

The respiratory quotient of the depancreatized animal assumes the characteristic low level of from 0.69 to 0.73 and is not raised when sugar is given. Under certain conditions in animals that have previously received a high protein diet and insulin, the quotient may be somewhat higher. The low quotient may indicate combustion of fat, but if any process, such as conversion of fat to sugar, which gives a very low quotient, should be taking place the quotient might indicate the resultant between sugar combustion, fat combustion and the conversion. When the pituitary gland is removed from the depancreatized dog, the quotient is raised. When the liver is removed from a depancreatized dog, the quotient also rises, indicating either that relatively more sugar is being burned or that conversions giving a low quotient are taking place to a smaller extent. Since more than one interpretation of a quotient is possible, great caution must be observed in drawing conclusions with regard to its significance. This ratio is often used, because of its convenience, to describe the results of physiologic research, but the investigator who makes use of this "instrument of attack" should not be accused of believing in its unitarian significance unless he specifically states his position.

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While the glycogen content of the muscles of a depancreatized animal may be reduced below the normal level, appreciable amounts remain during the life of the animal. There is no diminution of heart muscle glycogen, and recently convincing evidence for an increase has been obtained. Liver glycogen falls to very low levels. A very slight increase in both muscle and liver glycogen can be produced by giving large amounts of sugar without insulin.

The excretion of phosphate is increased in the depancreatized animal. The administration of sugar or epinephrine does not cause the prompt fall in the inorganic phosphate of the blood observed in normal animals. These results suggest that sugar may produce its effect through liberation of insulin, but in the light of the effect of raising the blood sugar on the rate of sugar production by the liver in depancreatized dogs receiving a constant amount of insulin, the latter organ as well as the pancreas comes under suspicion.

The diabetic animal is very susceptible to infections, but it is not established that this is due to the raised sugar content of the tissues. The specific antibodies are not significantly altered in amount, but other defense mechanisms may be made less effective by the abnormal metabolic condition that exists. Pathologic conditions are observed with considerable frequency in the eyes of diabetic animals. The liver may undergo extensive fatty degeneration and there may be an accumulation of very large amounts of neutral fat. Dietary factors play a large part in determining the extent of this change.

While there is considerable variation in the length of life of the depancreatized dog or cat, most individuals fed on a mixed diet do not live for more than two weeks without insulin. It is now established, however, that when the anterior pituitary is also removed the animal (dog) may live for at least a year and exhibit at most only a mild form of diabetes. Severe diabetes is produced under these conditions by administration of the diabetogenic substance of the anterior pituitary, but the maximum duration of this form of diabetes is not yet established. The condition is alleviated by insulin. Since the hypophysectomized pancreatectomized dog has apparently retained considerable ability to metabolize sugar (dextrose tolerance tests may give normal results), and the liver and muscle glycogen are within normal limits, it must be admitted by all that the pancreas is not essential to sugar combustion or glycogen formation under certain conditions at least.

These facts suggest to the physiologist the following classification of the diabetic state.

1. Increased glyconeogenesis due to lack of insulin; i. e. hypo-insulinism.

2. Increased glyconeogenesis due to excess of the diabetogenic substance of the anterior pituitary or in part perhaps to hyperactivity of the adrenal [2] or thyroid glands.

3. Increased glyconeogenesis not attributable to endocrine disturbances. While several factors, i. e. nerve impulses, products of infection, or changes in acid-base equilibrium, may affect the liver cells directly, endocrine disturbances may perhaps be an inevitable concomitant or result of these abnormal conditions. For this reason it is by no means certain that a diabetic state due solely to liver disturbances will be encountered. A type of hypoglycemia, however, attributable to extensive damage of liver cells, is recognized, and there are already certain bits of experimental evidence suggesting that the reverse, i. e. an overactivity, may be produced—possibly in some cases as the first stage of injury but conceivably, in other instances, by more physiologic mechanisms.

While it is possible to produce 1 and 2 experimentally as separate entities for a time, at least, it is probable that overlapping of the factors causing overproduction may occur clinically. In each of these three types there may be an under-utilization of dextrose by the tissues. This under-utilization may be, as many contend, the primary disturbance, but, on the other hand, it may be secondarily produced by the products of abnormal metabolic conditions of the liver. The favorable effect of insulin throws very little light on the factor or factors responsible for the overproduction or under-utilization.

EFFECTS OF THE ANTIDIABETIC HORMONE

It is well established that insulin restores to the depancreatized animal its ability to metabolize sugars and fats in a normal manner. The excessive breakdown of protein is prevented. The ketosis rapidly disappears. Glycogen accumulates in large amounts in the liver. Muscle glycogen may be increased. The respiratory quotient rises when sugar is made available, or in fact when insulin alone is administered. Animals recover their ability to deal with infective agents. In brief, a well treated depancreatized animal is difficult to distinguish from a normal one. There is always the difficulty, of course, that in the animal without a pancreas relatively large amounts of insulin are made available two or three times a day, while in the intact animal small or large amounts are presumably liberated from the pancreas as the need arises or conceivably at an approximately constant rate. Adult depancreatized dogs on an adequate diet [3] including the enzymes of the external secretion of pancreas have been maintained in good condition for more than four years. It cannot be stated, however, that these animals enjoyed at all times the fullest health, and there is ample opportunity to effect improvements in the details of treatment.

SOURCE OF INSULIN

While it is reasonable to suppose that small amounts of insulin are present in tissues other than the pancreas, methods are not yet available for their detection. Blood provides an exception to this generalization, but the active substance is detected by the intravenous administration of the whole blood and not by extraction of the insulin from the tissue. At least six groups of investigators, including the early workers on insulin in Toronto, were led for a time by errors in testing and by artefacts to believe in the wide distribution of appreciable amounts of insulin. In the mammalian organism the pancreas appears to be the only organ that manufactures or stores insulin.

The alpha and beta cells of the islands of Langerhans have been extensively studied and a third type, the gamma cell, has been detected. The beta cells, which occupy the periphery of the islets and whose granules are soluble in alcohol, are thought to be the source of insulin.

The main points of evidence which indicate that insulin is produced in the islet cells are as follows: 1. The active substance is found in degenerated pancreas

2. The alleged relationship of the adrenal to carbohydrate metabolism is discussed more in detail in the papers by Rogoff (The Adrenal Medulla, J. A. M. A. **104**: 2091 [June 8] 1935) and by Loeb (The Adrenal Cortex, J. A. M. A. **104**: 2177 [June 15] 1935) in this series.—ED.

3. Evidence is accumulating that certain accessory food factors may exert an appreciable effect on the intensity of glycosuria in pancreatic diabetes.

in which the loss of acinous tissue has proceeded much more rapidly than that of the islet cells.[4] Ligation of the pancreatic ducts eventually produces a decrease in the insulin content of the pancreas, but, when very few enzyme-producing cells remain, moderate amounts of insulin may still be extracted. 2. There are relatively large amounts of insulin in the principal islet of teleosteal fishes, in which few enzyme-producing cells are found;[5] 3. Histologically, the islets are glandular structures the obvious outlet for the secretion of which is through the blood stream. 4. When large amounts of carbohydrates are given to partially depancreatized dogs, characteristic lesions (hydropic degeneration) are found in the beta cells, which disappear when the carbohydrate is eliminated from the diet or is balanced by insulin. 5. In the clinical condition known as hyperinsulinism, the pancreas liberates abnormally large amounts of insulin. In many of these cases there are definite tumors of the islet cells. After the operative removal of these masses of islet cells the blood sugar is maintained at higher levels.

LIBERATION OF INSULIN

The arrangement of the capillary loops about the islet cells and the reported scarcity of lymph channels provide morphologic evidence in favor of the capillary blood stream as the pathway by which insulin reaches the systemic circulation. It is important to remember that insulin passes first to the liver.

While there are many pieces of experimental evidence which support the conclusion that the level of blood sugar is an important factor in the regulation of insulin liberation, the possibility that a decrease in the rate of discharge of sugar from the liver may also be produced when the blood sugar is raised is frequently overlooked. Increased deposition in or utilization by muscle is probably not an important factor in these very short experiments. When insulin liberation is maintained at a constant level in the depancreatized animal, the curve of blood sugar following an injection of dextrose may be very similar to that obtained in an intact animal. Removal of the liver produces the diabetic type of curve.[6] However, the injection of small amounts of dextrose into the artery supplying a pancreas grafted into the neck of a depancreatized dog or into the pancreatic artery in a decerebrate cat causes a prompt lowering of blood sugar. In the latter case the effect was not obtained when the splenic or portal vein was used. If these results on decerebrate cats can be accepted, they provide evidence for the chemical control of insulin liberation through an action of the dextrose on structures within the pancreas, but the effect of a raised blood sugar on the rate of discharge of dextrose from the liver must also be considered. The results of experiments with denervated pancreatic grafts suggest that the pancreatic effect is exerted directly on the islet cells. These manifestations indicate that the nerve control is not essential. The nerve impulses that affect the islet cells are apparently conducted by the vagus. Vagus fibers have been traced to the islet cells, and nonmedullated branches are said to pierce them. The results of stimulating the vagus appeared to be clear cut and the pathway was traced by one group of investigators to the hypothalamic region, but other workers have as yet been unable to confirm these observations. The effect of vagus impulses on the rate of sugar production by the liver requires further investigation, but the possibility that this mechanism is the one effective in lowering blood sugar must be considered.

THE MECHANISM OF ACTION

In the diabetic patient there is evidence that insulin enables more sugar to be burned, since the oxygen consumption is increased and the respiratory quotient rises. Some of the dextrose that disappears may be accounted for by the rise in liver glycogen, and there may be an increase in muscle glycogen. Increase of glycogen and rate of oxidation apparently account for all the sugar that disappears. The decreased nitrogen excretion indicates inhibition of glyconeogenesis.

In the normal animal the slight increase in oxidation and the deposition of glycogen in muscle apparently account for practically all the sugar that disappears. In adult animals of all the species that have been studied, liver glycogen does not increase.[7] The increase in liver glycogen in young rabbits is a secondary effect, probably due to liberation of epinephrine. It has been argued that the deposition of muscle glycogen represents only an effect of abnormally large amounts of insulin, but small doses do not cause the disappearance of sufficient dextrose, in addition to that which is oxidized, to provide building material for the minimum glycogen increase, which can be accurately determined. Convincing direct evidence that large doses of insulin inhibit glyconeogenesis in the normal animal is not available, but this possibility is strongly supported by the results of several series of experiments.

INTERFERENCE WITH THE ACTION OF INSULIN

Other Hormones.—There are five internal secretions the action of which may be considered to be antagonistic to that of insulin. There is no evidence of any chemical interaction of these hormones with the antidiabetic substance. Epinephrine causes a prompt mobilization of liver glycogen and probably somewhat later the conversion of muscle glycogen to lactic acid, which is in turn converted to dextrose or glycogen or both in the liver. The suggested action of epinephrine in inhibiting oxidation of dextrose is not well supported by experimental evidence.[2]

Removal of the adrenal cortex leads in some species to hypoglycemia, which is alleviated by injection of extracts secured from cortical tissue. The mechanism of action of such extracts is not established.[2]

Thyroxine, by making liver glycogen more easily mobilized and also probably by accelerating glyconeogenesis, tends to produce hyperglycemia. On the other hand, the increased oxidation of dextrose in the tissues of a thyroxinized animal exerts the opposite effect on blood sugar. In the first stages of hyperthyroidism there is a hyperglycemia and a decreased effect of insulin. In the later stages there may be severe hypoglycemia without insulin and a great susceptibility to the antidiabetic substance.[8]

While posterior pituitary extract raises blood sugar and interferes with certain of the actions of insulin, it is not established whether the oxytocic or the pressor principle or both exert the effect. Furthermore, the evidence as to whether or not posterior pituitary extract acts through the adrenals is still controversial.

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In certain species, at least, the diabetogenic substance of the anterior pituitary appears to be a very powerful antagonist of insulin.[9] Hypophysectomized dogs, even after removal of the pancreas, may exhibit profound hypoglycemia. They are very susceptible to insulin. The information at present available indicates that the liver is essential to the action of the diabetogenic substance, which apparently acts, in large part at least, by stimulating glyconeogenesis.

Enzymes. — Insulin is destroyed by pepsin-hydrochloric acid and by the activated proteolytic pancreatic enzyme. The pancreas may, however, be incubated aseptically at neutral or acid reaction without loss of the antidiabetic substance. Insulin is relatively unstable in alkaline solution. There is apparently an enzyme system in blood which is capable of activating insulin, but its characteristics have not been extensively studied.

Reaction of Tissues.—Since insulin acts on the cells of the liver and muscles, factors that influence these tissues, acidosis for example, may modify insulin action. Furthermore, since the liver is so largely responsible for the regulation of blood sugar, influences affecting this organ may cause a change in sugar content quite apart from the action of insulin. A change in the acid-base equilibrium of the body toward the acid side renders injected insulin less effective.

Products of Infection.—The toxic products elaborated by many micro-organisms may interfere with the action of insulin. There is experimental evidence (1) that the insulin content of pancreas is decreased in certain severe infections, but this does not necessarily indicate a decreased rate of liberation of the hormone; (2) that the adrenal and thyroid glands are stimulated to release more of their internal secretions, and (3) that the synthesis of glycogen from lactic acid in the liver is inhibited. Certain toxins may act on one or more of these mechanisms, but investigation of this field is still in the preliminary stages.

Anesthetics.—All anesthetics interfere more or less with the action of insulin. More or less asphyxia is produced by all general anesthetics. In asphyxia acid products tend to accumulate. Chloralose and amytal cause less disturbance of carbohydrate metabolism than some other anesthetics.

HYPERINSULINISM

The tendency to refer to all clinical cases of spontaneous hypoglycemia, which may be due to (1) liver injury or to (2) deficiency of anterior pituitary secretion, adrenal insufficiency or other causes, as well as to (3) liberation of excessive amounts of the internal secretion of the pancreas, as hyperinsulinism should be combated. The signs of hypoglycemia in these various conditions may of course be identical, but hyperinsulinism is established only when removal of a tumor of islet cells corrects the condition. It is possible that general hyperplasia of islet tissue is responsible for some cases of hypoglycemia, but further study is needed to settle this point. When a large part of the pancreas is removed and the hypoglycemia is alleviated, which is the desired clinical result, the finding does not prove that the internal secretion had been liberated in abnormally large quantities. The same result would have been secured if the hypoglycemia was due, for example, to diminished secretion of the diabetogenic substance of the anterior pituitary. The hypoglycemia produced experimentally by extirpation of the anterior pituitary may be alleviated by complete removal of the normal pancreas. By this means two endocrine factors influencing the production and utilization of sugar in opposite directions are balanced at a new and lower level.

The signs of hypoglycemia have been frequently described. Attention has been drawn from time to time to chemical substances, the accumulation of which was thought to be responsible for these signs, but further study has failed to support the early observations. There is no convincing evidence that a toxic chemical substance accumulates when the blood sugar is maintained at low levels. The typical signs of profound hypoglycemia are dependent on the loss of integrity of nerve cells in the higher centers of the brain. There are no physical signs of hypoglycemia in the spinal animal or in one anesthetized by a general anesthetic.

CHEMISTRY OF INSULIN

The most active form of insulin is that obtained in the crystalline form (Abel).[10] This material is composed of numerous amino acids (cystine, tyrosine, arginine, histidine, lysine, leucine, glutamic acid, proline and phenylalanine) and gives all the typical protein tests. It appears very unlikely that the active material is merely adsorbed on the crystalline protein. Recent work by Scott [11] has shown that the crystals are probably the salt of insulin with a metal such as zinc or cadmium. The free substance has not yet been obtained in crystalline form.

STANDARDIZATION

The potency of insulin is expressed in terms of the international standard powder, which contains 8 units per milligram. The crystalline preparation, which has a potency of approximately 25 units per milligram, is being substituted for the amorphous material. There will be no change in the size of the unit. Insulin should always be tested against the international or subsidiary standard. The lowering of blood sugar in rabbits or the production of convulsions in mice furnishes satisfactory effects of the hormone for the comparison of unknown and standard products.

SUBSTITUTES FOR INSULIN

Insulin therapy has two obvious disadvantages: (1) the transient effect and (2) the necessity for parenteral injection of the active material. The most important of the suggested substitutes is synthalin (decamethylene diguanidine). This substance does not increase deposition of muscle glycogen and the effect on hepatic glyconeogenesis is accomplished in a highly unphysiologic manner. Insulin is apparently the only agent that inhibits sugar formation without damaging liver cells. Extensive deposits of fat produced in diabetic dogs by fat feeding as well as by many chemical compounds other than synthalin interfere with sugar formation. It is preferable for the diabetic organism to excrete the large quantities of sugar made by a relatively healthy liver than to be made "sugar free" by damaging liver tissue so that less dextrose is formed.

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Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING ARTICLE AND REPORT.

HOWARD A. CARTER, Secretary.

THE INFLUENCE AND THERAPEUTIC USE OF HEAT

PHYSIOLOGIC EFFECTS OF HEAT

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The use of external heat in the sense ordinarily understood by that term was a familiar therapeutic procedure to the ancients of Greece and Rome, who constructed elaborate establishments for the practice of hydrotherapy in various forms and also made use of naturally occurring thermal springs, such as those still frequented at Aix les Bains. Notwithstanding the application of heat to an increasing variety of conditions, the manner in which it accomplishes its purpose has been, until recently, poorly understood, chiefly owing to the fact that the actual conduct of most physical therapeutic measures has been in the hands of persons untrained in medicine.

One of the outstanding phenomena, obvious even to the layman, in the systemic application of external heat is the more or less profuse sweat induced. This occurrence has given rise to the popular idea of "elimination," which has found great favor with the public and has even crept into medical writings in an uncritical way. The conception of what is eliminated has been vague, and small account has been taken of other and equally important changes induced. The last few years have been productive of new data however and, while much remains to be investigated, a fairly clear concept is now afforded of what occurs in the physiologic sense when the human body is exposed to heat.

According to Bazett,[1] radiant energy, to which the body is normally more or less exposed in the form of sunlight and also, in recent years, through artificial means, may be classed as (*a*) ultraviolet rays of short wavelength, 1,850 (artificial light), 2,900 (sunlight) to 3,600 angstroms; (*b*) visible light, from 3,600 to 7,500 angstroms; (*c*) near infra-red, from 7,500 to 15,000 angstroms; (*d*) intermediate infra-red, from 15,000 to 30,000 angstroms, and (*e*) far infra-red with wavelengths greater than 30,000 angstroms. Heat from radiating objects, such as steam or hot water radiators, hot water bottles and hot water baths, consists mainly of group *e*, and transmission to a depth is by conduction; when derived from sources such as lamps with a dull red glow, the main energy is probably in groups *d* and *e*, and conduction is still the main method through which deep effects may be attained. However, if sunlight or luminous sources of heat are employed, much of the energy may be in groups *b* and *c* and some deep effects will result through direct transmission of the radiant energy to a depth.

According to Bazett,[2] the rate at which changes of temperature penetrate is relatively slow, the heat capacity of the tissues is high, and relatively large quantities of heat have to be transported before the temperature is greatly altered. The tissues can be warmed, however, up to a temperature of 98.6 F. with relative rapidity; venous blood in its return carries heat inward and does so the more rapidly the greater the extent of the vasodilatation; in addition, the increased arterial blood supply warms the tissue at the expense of the rest of the body.

In a cold environment the conditions are simpler, but the thermal conductivity is diminished as the result of the vasoconstriction induced. Zondek [3] reported that an icebag in close apposition to the thigh caused a fall of temperature at a depth of 50 mm. from 98.8 to 97.3 F. in one hour when the skin had fallen to 44.6 F. in a subject with fat 25 mm. thick. In the case of a fat subject (fat 50 mm. thick) an icebag applied to the abdomen for one and one-half hours caused a fall of the skin temperature to 42.8 F., but the temperature of the abdominal muscles at a depth of 50 mm. fell only from 99.7 to 96.8 F.

In his study of the effects of abdominal thermal applications on the dog's intraperitoneal temperature, Brill [4] observes that cold applications have little effect on the intraperitoneal temperature, the greatest fall noted being 2.5 degrees C., which was observed in one instance. Hot applications likewise produce no appreciable change. Such observations as these, which have been corroborated by Hepburn, Eberhard, Ricketts and Rieger,[5] strongly suggest that the beneficial effects of hot and cold abdominal applications are due to factors other than the effect on intraperitoneal temperature.

The effects of systemic exposure to heat from various sources are much the same in principle and will therefore be discussed together, except when certain differences necessitate particularization.

One of the earliest effects to be noted after systemic exposure to heat is that on the circulation. Thus, the pulse rate rises more or less proportionately to the rise in body temperature [6] in the ratio of about ten beats for 1 degree F.,[7] much as it does in fever.

The effects on blood pressure of external heat and cold are somewhat varied.[8] Some observers believe that all baths at a temperature much above or below that of the body raise blood pressure,[9] but in general in normal persons warm baths probably tend to lower blood pressure and cold baths tend to raise it. There are some exceptions to this rule, and a bath above 40 C. (104 F.) may give a blood pressure above normal, while a cold bath may occasionally induce a temporary fall in blood pressure preceded and followed by a rise.[7] If exposure to external heat is in the form of a bath, there takes place, in addition, a diuresis dependent on the immersion of the abdomen in the water.

Systemic exposure to external heat generally produces a more or less well marked hyperpnea or overventilation of the lungs. This increases roughly parallel with the rise in body temperature, and water vapor is lost in large quantities through the expired air. Systemic exposure to heat in any form results, therefore, in a loss of fluid from the body through the lungs and sweat and, following baths, through the urine also. This causes a temporary loss of weight.[7] Following

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extreme sweating a slight concentration of the blood[10] tends to arise, but it is doubtful whether this takes place in any important degree under the usual conditions of clinical practice.[11]

Next to the kidneys the skin is, in man, the most important accessory channel for the elimination of water, and the salt excreted in the sweat may amount to ten times that normally present in the feces.[12] The sweat also contains, qualitatively, certain other substances occurring normally in the urine, such as urea, ammonia, uric acid, amino acids, creatinine, phosphates and sulphates,[10] and it may also contain dextrose. The elimination of these substances, especially water, salt and urea, forms the basis of the long-standing use of the sweat process in various forms of nephritis accompanied by edema or high blood urea nitrogen. There has been wide clinical belief in the value of this measure in nephritis, in which its influence is undoubted as regards salt and water. As regards the compensatory elimination of nitrogenous substances, there is some evidence to indicate it, but there are those who doubt "vicarious" excretion of nitrogen on the part of the sweat glands, and it seems that perspiration does not always lead to a decrease of urea in the urine.[13]

It is not generally appreciated that carbon dioxide, a chief end-product of metabolism, escapes through the urine and sweat, as well as through the lungs, and one of the most fundamental effects of exposure to heat appears to depend somewhat on the increased loss of carbon dioxide through these three channels. As a result of the rise in the body temperature or hyperpyrexia, the general body metabolism is increased and carbon dioxide is formed in quantities larger than normal. The overventilation through the lungs, however, washes out the carbon dioxide in even greater proportionate amounts. There also results from the heightened metabolism an increase in the phosphates and sulphates from the breakdown of protein, but these acid substances find their escape through the urine. In addition to the loss of all these substances, it has also been shown that the urine and the sweat contain fatty acids, including lactic acid, which are probably increased in amounts during exposure to external heat. The elimination of lactic acid through the skin during the sweating process constitutes one of the significant factors in the maintenance of the acid-base equilibrium in the body. Because of the low degree of ionization of lactic acid, the excretion of lactic acid and lactates results in the sparing of fixed base.[14] The sweat produced under the influence of heat, induced by the radiotherm in the cases studied, contains lactic acid in concentration greater than that of the blood.

The net result, therefore, of the loss of these various acid substances, chiefly carbon dioxide, is to leave a relative excess of alkali in the blood and probably in the tissues.[15] The blood becomes too alkaline, a systemic alkalosis results, and the excess of alkali is then eliminated through the urine and sweat until the normal acid-base equilibrium is restored. The urine and sweat thus generally change their reaction, becoming less acid, alkaline, or more alkaline. A sustained alkalosis may lead to tetany; it constitutes one of the sources of danger in the improper therapeutic use of external heat.[16]

A great loss of water and salt consequent on exposure to heat induces serious consequences unless this loss is partly compensated by ingestion. This loss may be one of the factors, together with the alkalosis referred to, which induce the severe cramps in the muscles occasionally seen among stokers and other workers in extreme heat. The clinical application of external heat with excessive sweating may likewise be followed by serious consequences. Water is usually given to the patient, and saline solution is occasionally administered to compensate for the losses of fluid and salt. It is obvious however that, unless the temperature and amounts of fluid are considered, the anticipated sweating and the benefits of it may be prevented or delayed.

The physiologic changes induced by local exposure of a part to heat are along the lines just described, but more intensive treatment is obviously possible because the process can be longer continued. Relaxation of tissues is induced, especially of the muscles, together with a hyperemia probably due to dilatation of blood vessels and a greater total blood flow in the area concerned. Another physiologic factor involved is the increased rate of transfer of fluid across the capillary wall during the vasodilatation induced by heat, as shown by Gibbon and Landis.[17]

Local sweating also takes place, and the tissues are put in a condition to benefit more than they otherwise would by such measures as massage and passive motion or even active motion. If the local use of heat is continued too long, a systemic response may take place, dependent on a general hyperpyrexia comparable to that following systemic exposure. This may be an advantage or a disadvantage, according to the conditions present, but must be considered in feeble patients or those already being exposed to systemic heat. The effects of heat locally will be further developed under the local use of heat in surgery.

A recent development in the use of heat is the artificial induction of fever. A variety of measures is useful to this end; namely, those already mentioned and those depending on exposure of the body to radiation, to induced electric fields and to the actual passage of the electric current through the tissues. The measure last mentioned is that which has been most fully studied.

Another means of producing much the same result is the injection into the body of material such as killed bacterial organisms, foreign proteins and the like, the reaction to which includes the production of fever. It is probable that the results achieved by these several respective measures, however, depend largely on common factors for their effects. The use of hyperpyrexia through diathermy[18] permits rather more controlled study of the conditions arising and is in other ways preferable in a majority of cases suitable for such therapy. The alterations of physiology achieved through it include, apart from the usual results of external heat, the change in the blood formula recognized to accompany the use of nonspecific protein reactions, as well as some other phenomena referable to disturbances of the nervous system and even of the renal system brought

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15. Cajori, F. A.; Crouter, C. Y., and Pemberton, Ralph: The Alleged Rôle of Lactic Acid in Arthritis and Rheumatoid Conditions, Arch. Int. Med. **34**: 566 (Oct.) 1924.
16. Cajori, Crouter and Pemberton.[11]
17. Gibbon, H. J., and Landis, E. M.: J. Clin. Investigation **11**: 1019 (Sept.) 1932.
18. Neymann, C. A., and Osborne, S. L.: Arch. Phys. Therap. **15**: 149 (March) 1934.

about through the higher and more sustained febrile state. The kidney occasionally experiences detriment, under vigorous applications, and this may result, in part, from damage to it by the high temperatures immediately adjacent to the organ itself. Similar considerations apply to the use of ultra high frequency induced electric fields which cause eddy currents in tissues with resultant heating effects. This procedure permits of deep penetration and can be used locally or systemically. It has the added advantage of obviating immediate contact with the patient.

The treatment of disease by means of hyperpyrexia originated with the use of the malarial parasite in dementia paralytica and has been extended to include a considerable variety of disease states. Omitting discussion of the therapeutic effects on diseases of the central nervous system, which will be considered elsewhere, the diseases chiefly submitted to this form of therapy have been various forms of arthritis and asthma.

The treatment of disease states by raising the body temperature through various electrical means is a powerful therapeutic measure capable of real benefit and also of undoubted harm unless carefully controlled. At the present time, therapy of this nature should be conducted under hospital auspices.

FORMS OF APPLICATION

Dry Heat.—The various means and methods of applying physical therapy in almost any of its forms constitute specialties in themselves, and within the small compass of the present article only those features can be considered which are essential to a general understanding of the subject.

Apart from the familiar hot water bag, the most common mode of application of dry heat is that afforded by the electric light bulb. For local application, the apparatus usually takes the form of a parabolic mirror, suitably mounted, with the lamp at the focus so that the issuing rays are parallel. The apparatus can be held in the hand, or it is mounted on a stand and can be directed toward any part. For more intensive local use a boxlike container, with or without an internal reflecting surface, open at the ends and equipped with light bulbs, is placed over the limb or part, with the patient in the sitting or the reclining position.

For systemic exposure, lamps are usually placed within a "cabinet" or large box containing a reflecting interior surface and large enough to allow the subject to sit on a chair, the head emerging through the doors or other covering at the top. The number of lamps in such an apparatus may be from twenty to fifty or more, subject to control in small groups. For exposure in the recumbent position, the lamps are placed within a troughlike semicircular container, also bearing a reflecting interior surface and about 5 feet in length. This is placed, with the concave side down, over the subject, whose head is allowed to emerge at one end. Blankets are placed over the whole and drawn snugly around the neck and face in order to prevent undue radiation.

Dry heat is also administered in the form of hot air, but this usually requires elaborate equipment for the purpose of heating the air and is hardly available to the general practitioner, except in a few institutions. Electrical resistance coils placed within a boxlike container also afford a useful means of obtaining dry heat, especially for application to limited areas such as a knee or an ankle. These various forms of apparatus can all be obtained on the market under various trade names, and they can be improvised at home with excellent results when necessity demands. Dry heat of lesser intensity can also be supplied for local purposes in the form of a resistance coil of flexible wires, properly insulated and covered with cloth, for such uses as those to which the familiar hot water bag is put.

One of the most important uses of dry heat in a local sense is that afforded by the actual cautery, which may be heated by flame or fire, as in the old days, or, more appropriately, by the electric current. The chief use of this is for destructive purposes in dermatologic conditions, including new growths, and will be discussed under that heading. The actual cautery has also long been used as a "counterirritant" in sciatica, though less so now than formerly. Probably some of its effects are due to the reaction from protein split products and the "shock" of the burn.

Hydrotherapy.—Probably the oldest form of the systemic application of heat is the hot bath. The presence of thermal springs scattered throughout the world has given rise to elaborate establishments for their utilization, but as far as heat per se is concerned almost equally satisfactory results can be obtained in many instances by the simplest forms of apparatus, such as the ordinary bath tub. The water used may be pure or it may contain various salts or other substances, such as magnesium sulphate or carbon dioxide, intended to increase or add to the effects. The temperature of the water varies, of course, according to the purpose of the bath, and this question will be considered under therapeutic indications.

Next to the hot bath, the most frequently employed form of moist heat is that afforded by the so-called hot pack. This consists in principle in wrapping the body in a sheet or blanket made hot by being dipped in hot water of about 82 C. (180 F.) and subsequently wrung out more or less thoroughly. Obviously the severity of application will depend on the temperature of the enveloping sheet or blanket, and this effect will be further influenced by the number of blankets superimposed on the subject to prevent evaporation and cooling. Occasionally, the sheet or blanket placed on the body is below body temperature, constituting the "wet pack," under which circumstances the effect of heat is achieved through a conservation of the body heat by wrapping the subject with many blankets to prevent as much evaporation as possible.

Another form of exposure to moist heat is the steam bath, although this is by no means so widely employed as the hot water bath. A home-made apparatus can usually be "rigged up" in any household by means of large steam kettles, an oil lamp and a frame to elevate the bedclothes. The steam "room" has long been in use and consists simply of a chamber into which steam under low pressure is allowed to escape. The disadvantages here are that the patient must breathe the hot moist air, and a better form of application is that in which the subject sits in a cabinet or lies in a sort of box with his head outside. There is some danger, however, in this procedure, as burns have occasionally been caused by faulty steam pipes or joints. In some instances, electric resistance coils supply steam under low pressure in a manner well adapted to this purpose.

The mud bath is an old form of application of moist heat but, in general, depends on the availability of certain soils, heated by thermal springs or artificially, and need hardly be considered at length here.

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The forms of wet heat that have been described are used chiefly for systemic treatment, but a useful local application of moist heat can be made by means of the so-called whirlpool bath. This consists of a receptacle of suitable shape, usually deep and rather narrow, containing warm or hot water made to circulate rapidly by means of a laterally placed water jet. The part to be treated, usually an arm or a leg, is placed within the receptacle, and the temperature of the water is gradually raised to the desired point. The motion of the water intensifies the effect of the heat for any given temperature and has other advantages through its impingement on the tissues.

THERAPEUTIC INDICATIONS AND PRACTICE

The therapeutic indications for the use of external heat can be grouped under the two general headings of general exposure and local exposure, according to whether a systemic or a local effect is desired. Systemic effects find their application for the most part in medical, as contrasted with surgical, conditions and have been widely used in the following disease states or syndromes: nephritis, acute or chronic; arthritis and rheumatoid conditions, in which either local or systemic heat or both may be used; and neurologic conditions, including neurasthenia, functional psychic disturbances and the true insanities.

The therapeutic indications for the use of heat locally are chiefly in the following fields: surgery, especially orthopedic, following fractures, dislocations, sprains, cicatrization after operative procedures and the like; and arthritis, when a limited influence on a joint or joints is desired.

NEPHRITIS

There is probably no other condition in medicine in which the systemic use of external heat has been longer thought to have consequences of value than that of nephritis. Whatever other pathologic manifestations may accompany nephritis, certain symptoms demanding treatment are apparently dependent on the retention of toxic material, possibly of a nitrogenous nature, salt or water, and acid products of metabolism, especially phosphates and sulphates.

As already pointed out, some workers doubt the vicarious removal of nitrogenous substances through the skin, when elimination through the urine is reduced, but clinical experience is in favor of the view that something of this nature may occur. Furthermore, it is possible that some other toxic substances the nature of which is not yet known may be removed at the same time. It is well recognized, however, that the degree of toxicity does not run precisely parallel with the accumulation of nitrogenous substances. Thus, patients with uremia may show a disproportionately small rise in the urea nitrogen and, on the other hand, patients with marked increase in the urea nitrogen may present few or no clinical evidences of intoxication. Again, the figures for the "urea clearance" test may fall as low as 20 to 40 per cent in the presence of a normal blood urea.[19] It is safe to say, however, that in nephritic conditions accompanied by marked laboratory evidences of retention of nitrogen, or by clinical evidences which suggest the toxemia consequent on such retention, the sweating process is to be considered. There is some evidence that in conditions accompanied by retention of blood nitrogen the sweat may contain nitrogen in amounts larger than normal.[20]

The argument has been advanced that, in the presence of toxemia from renal insufficiency and retained nitrogen, sweating serves only to concentrate the blood and to add to the danger from the retained substances.[21] There is some doubt as to the validity of this, however, as the blood maintains its water balance with great tenacity, drawing on the tissues for this purpose, and the evidence is not final that under conditions of ordinary therapeutic procedure the blood undergoes any true concentration.[8] Furthermore, in the absence of inability to excrete water there would seem to be no objection to the administration of fluid to prevent concentration, as is indeed the practice in many hospitals. It is to be borne in mind, however, that the elimination of water constitutes one of the functions of the kidney, and, as O'Hare[22] points out, a further burden may be added and even pulmonary edema may arise from undue administration of fluids.

Finally, it should be stated that the results believed to be achieved may be due to changes induced by heat in the blood flow, to an alteration of metabolism, or, in nephritis accompanied by acidosis, to the production of a systemic alkalosis as already described. Whatever the mechanism and whatever the difference of opinion as to the theoretical benefits to be obtained, however, it is probable that some experienced clinicians would be unwilling to withhold application of the sweat process as a practical method of treatment in the toxic nephritis under discussion.

Another phase of renal dysfunction in which the sweat process has long been regarded as of value is that accompanied chiefly by retention of salt and water. While the bowels may be made the channel for elimination of water in large quantities by hydragogue cathartics, water can be eliminated in equal or even greater amounts through the sweat. Evidence has been presented that salt may be removed through the sweat channels in amounts equal to or larger than those occurring in the feces.

In the presence of edema or anasarca of renal origin, the hot pack or general body bake may at times have significant consequences and the loss of fluid from the tissues may be obvious almost from the start. Usually, however, many treatments are required.

The practice of giving sweat baths in nephritis is less common than formerly. The modern view of therapy in chronic Bright's disease is directed toward the elimination of toxins which, in passing through the kidney, may aggravate the renal lesion. This means the eradication of infection, proper elimination from the bowel, and finally a diet so devised as to avoid undue strain on the renal system by all products of excretion. This, of course, may include the ingestion of water. It would appear that proper adjuvant use of the sweat channels would be complementary to the foregoing procedures, but the problem is fraught with many difficulties that have not been wholly threshed out.

In all these conditions the physician must be guided by good judgment in the application and severity of the measures used. The guiding principle must be

19. Beaumont, G. E., and Dodds, E. C.: Recent Advances in Medicine, Philadelphia, P. Blakiston's Son & Co., 1934, p. 49.

20. Cajori, Crouter and Pemberton: Ann. Int. Med. **2**: 1243 (June) 1929.

21. Textbook of Medicine, edited by Cecil, R. L., and Kennedy, Foster, Philadelphia, W. B. Saunders Company, 1927.

22. O'Hare, J. P.: The Treatment of Chronic Bright's Disease, J. A. M. A. **103**: 1373 (Nov. 3) 1934.

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that benefit can be forthcoming only when the patient is in a position to withstand treatment of such severity and respond to it, and the physician must be on his guard lest contraindications appear, such as cardiac decompensation, circulatory collapse or high fever. It is sometimes necessary, however, to push treatment even in the presence of such contraindications.

The particular manner in which heat is systemically applied in nephritis is of secondary importance; but the simplest form, and one that can be carried out in any household, is the hot pack already briefly mentioned. This properly comes under the topic of hydrotherapy, however, and the further details of its application will be discussed there.

Considerable prostration may occasionally follow the general procedure referred to; and, furthermore, although the effect of any one "bake" may be inappreciable, the effect of many treatments is sometimes cumulative. In few diseases is any single measure to be regarded as the only one to be relied on, and this is eminently true of the use of the sweat process in nephritis. The use of the skin as an emunctory organ must be accompanied by full use of the other channels, especially the bowels, and by such medication and control of protein, salt and fluid intake as modern conceptions of medicine require.

The systemic application of heat is beneficial in meeting the conditions generally included under the head of shock. In this connection mention should perhaps also be made of the use of the mustard bath or the mustard pack, especially in relation to collapse in infants. Some clinicians [23] believe that there is no medicinal agent, with the exception of epinephrine, which is so dependable. The water should approximate 105 F., and mustard should be added in the amount of a heaping tablespoonful to each quart of water. Care must be exercised to protect the eyes of the patient, and constant friction should be maintained while the subject is in the tub. Baths of this general nature are useful also in relation to the convulsions which children experience, but this subject properly belongs under the use of heat in diseases of the nervous system.

Heat in the form of hydrotherapy has long constituted part of the process known under the name of the Nauheim bath, extensively used at Nauheim, Germany, in relation to cardiac disorders of various kinds. The temperature of the water begins at 92 F., and the measure in general can therefore be properly placed in the category of systemic heat. The benefit to be derived by the Nauheim bath is a matter over which there is much difference of opinion. The beneficial consequences alleged to arise have been referred to the carbon dioxide content of the water and also to the friction employed while the subject is in the bath, as well as to various other factors, such as rest and change of scene.

It must be confessed that the favorable clinical evidence adduced by those who have the greatest familiarity with this form of treatment is considerable, and it is also only fair to say that the conditions which obtain at Nauheim cannot necessarily be duplicated elsewhere through the use of artificial baths of the same general nature.

This form of treatment has never had very wide use in the United States, and it would profit by further study at the hands of disinterested observers.

23. Ward, J. B.: Arch. Pediat. **45**: 556 (Sept.) 1928.

ARTHRITIS AND RHEUMATOID CONDITIONS

The field in which the application of external heat, both systemically and locally, has its most extensive and varied application is probably that of arthritis and rheumatoid conditions. The full benefits to be derived from the systemic use of heat in this connection are not always forthcoming from the heat alone, however, and sometimes depend on contrasting and accessory applications of cold. The latter phase of treatment constitutes an essential part of hydrotherapy, and the details of the conduction of this measure in its various forms will be considered in the section devoted to that topic. The matter will be discussed here sufficiently merely to indicate the general application of heat to the rheumatoid syndrome.

In view of the considerable confusion that still exists regarding the nomenclature and classification of the arthritides, as well as of the underlying pathologic changes concerned, there is no stereotyped guide to be followed in selecting cases appropriate for this treatment.

Those patients who are fairly robust afford the best opportunity for this practice. It is important to remember that systemic exposure to heat in any form may occasionally have distressing consequences, either immediately or after a course of treatment, and it is therefore essential to exercise caution in subjecting to such treatment patients who are ill equipped to stand it. Those forms of arthritis which are thought perhaps to withstand such therapy best and to benefit most from it are cases of the degenerative or so-called hypertrophic type in middle aged, well nourished women, although the proliferative or so-called atrophic type may be equally helped. It must be pointed out here, as in connection with nephritis, that exposure to heat or hydrotherapy constitutes only one measure of treatment in the rheumatoid problem and must not be followed except in correlation with other established principles of treatment. Especially is this true in relation to the important influence of focal infection. A patient with arthritis should not be subjected to the measure under discussion unless and until a complete medical examination has indicated the justifications and indications for it. For generations the public has frequented sanatoriums of all kinds where these measures have been applied in a wholesale way with the result that, although these measures have undoubted therapeutic value, failure and detriment also have followed.

As mentioned in the section on physiology, belief in the value of "elimination" in this disease has long been popular, but there is only limited evidence to support this as an important factor in itself. Elimination of water [24] in the form of sweat may in itself contribute to a betterment of the disturbances of physiology accompanying the rheumatoid state. The possibility that a low-grade "edema" of some tissue accompanies certain phases of the arthritic syndrome cannot be dismissed from consideration. There is, however, definite evidence that some of the other effects achieved by exposure to heat play an important rôle in the treatment of arthritis. These effects are chiefly those arising from the heightened circulation and the increased metabolism induced. Evidence of changes in the circulation is to be seen in the obvious influence on the skin capillaries of the contrast baths or douches so success-

24. Pemberton, Ralph, and Scull, C. W.: M. Record **140**: 653 (Dec. 19) 1934.

fully used in institutional treatment at the conclusion of the "bake" or hot bath. A true "metabolic whip" is afforded by cold water properly used.

This procedure has application to a variety of debilitating conditions; thus, Knopf in his "Report to the United States Government on Tuberculosis with Some Therapeutic and Prophylactic Suggestions," expresses the opinion that a judicious course of hydrotherapy is of value in helping to "strengthen the cutaneous and nervous systems against the changes of temperature" and has prophylactic value toward the development of "colds" among certain classes of tuberculous patients.

The "bake" or bath may be given alone, however, in which case profuse sweating is induced and the subject is allowed to rest for an hour or more to compensate for the somewhat debilitating effects; or, more frequently, the exposure to heat is briefer and sufficient only to inaugurate or induce a mild diaphoresis. Following this procedure, which is generally administered with the patient in a sitting posture, a "tonic" shower or douche is given, beginning considerably above body temperature and shortly reduced to slightly below body temperature. This is best accomplished by an attendant who directs on the patient a jet of water, the temperature of which is under control. An exposure of about eight minutes to the electric cabinet "bake," followed by a so-called scotch douche or other form of cooling hydrotherapy, permits the subject to go at once out into the air with a sensation of exhilaration and well being instead of lassitude. There is also exercised at the same time an influence on the nervous system, which in the end may be quieted by the process described, notwithstanding the apparent "shock" of the cool or cold water. Even persons of robust constitution should be subjected only gradually to these procedures; but by beginning cautiously even highly asthenic types can be educated to stand them and be benefited by them.

The sweating process alone, without the cooling contrast shower, is easier of attainment and can be brought about by means of the hot pack or hot bath in almost any household. In many instances the metabolic stimulus given by this single procedure is of great value and should be utilized when circumstances justify it. Some of the effects of cooling hydrotherapy can be achieved by means of the bed sponge or bath, but care must be used to avoid chilling. If the sweating process is prolonged and perspiration is profuse, the patient must rest for an hour or more before rising, or depletion and fatigue will result.

The general regimen briefly outlined can be carried out more or less successfully in the home, but the full achievement there of such results as follow the conduction of these measures by skilled hands in adequately equipped institutions can hardly be expected.

Much of the benefit of treatment at institutions is made possible by the incidental removal of the patient from causes of worry and fatigue, and to this can often be added the stimulus of new surroundings.

Some further mention must be made of the influence of induced fever,[25] probably most conveniently achieved in the rheumatoid syndrome through diathermy. The whole subject of the influence of induced fever on various disease states is still far from being thoroughly understood, and this limitation applies equally in respect to the treatment of arthritis by means of it. There is some evidence to indicate, however, that in certain phases of the arthritic syndrome, especially perhaps the more acute states, beneficial results may follow the induction of sustained fever up to 104 or even 106 F. Differing uses of nomenclature as well as uncertainty as to diagnosis make it difficult to attach finality to the value of the beneficial results reported to date. Gonorrheal arthritis has also been reported, on more substantiated evidence, to be benefited. In view of the varied etiology of arthritis, however, conservatism should be exercised in applying this potent measure indiscriminately to large groups of cases, in that many of them are asthenic and poor candidates for radicalism of any sort.

25. Jones, A. C.: Arch. Phys. Therap. **15**: 149 (March) 1934.

LOCAL APPLICATION OF HEAT IN ARTHRITIS

The application of external heat locally to a joint or joints in arthritis is often of the highest value. The principle obtains here, as elsewhere, that reliance must not be placed on this measure alone. It must be considered in conjunction with other principles of treatment of the disease as a whole, and the joint in particular. The measure most often used in conjunction with local external heat in arthritis is massage and, although often misused in ignorant hands, it constitutes an almost necessary adjunct to the use of heat alone, especially in the form of effleurage. The forms of heat available for local use are discussed at the beginning of this article. The value of the heat can sometimes be enhanced by incorporating with it some other principle, as in the use of a hot saturated solution of magnesium sulphate applied to the affected part and kept hot by repeated application or a radiant lamp. This procedure sometimes greatly relieves pain. Application of heat should not be carried to the point of irritation and should depend for its effects on repeated use, once or twice a day, over a period varying from about ten minutes to half an hour. The temperature within the apparatus should not be above about 82 C. (180 F.), or the duration of treatment greater than twenty minutes at the outset. Temperature and length of exposure can be slowly increased. Local sweating generally occurs, and the part should be kept warm after the treatment. If a region such as the shoulder is baked for a long period, a systemic reaction may occur comparable to that following systemic exposure, the results of which may be depleting or otherwise undesirable.

Heat is of value also in disturbances of circulation in the peripheral vessels, such as thrombo-angiitis obliterans, diabetic gangrene, Raynaud's disease and intermittent claudication. Heat has been recommended systemically [26] in thrombo-angiitis obliterans to control pain but can be more conservatively used locally.

In advanced peripheral vascular diseases, Starr [27] recommends heat at an "optimal temperature" in conjunction with rest, desiccation and exposure of the part to oxygen. A temperature of from 33 to 35 C. usually relieves pain and is preferable to less controlled variations.

There may also accrue a beneficial effect on the indolent lesions often encountered in such conditions. Coincident care of the underlying state is of course imperative. Contrast baths may have value when the local vascular function permits.[28]

26. Stroud, W. D.: Year Book of General Medicine, 1934, p. 628.
27. Starr, Isaac, Jr.: Am. J. M. Sc. **187**: 498 (April) 1934.
28. Perlow, Samuel: Ann. Int. Med. **8**: 743 (Dec.) 1934.

BURDICK SHORT WAVE DIATHERMY MACHINE (SWD-5) ACCEPTABLE

Manufacturer: The Burdick Corporation, Milton, Wis.

This unit is recommended for medical diathermy as used for producing heat within the body tissues, and for surgical diathermy. The apparatus is available in either cabinet or portable style. The machine is of the single tube, simple oscillating type. Raw alternating current is fed into the plate circuit and thus only the positive half of the alternating current, 60 cycle, is used. Proper tuning to resonance, in conjunction with the relative power output of the patient's circuit, is indicated by a milliammeter of the thermocouple type. A protective circuit breaker switch is provided to guard the vacuum tube oscillator against injury to excessive variations in line voltage and line surges.

Burdick Short Wave Machine.

Under full load this unit was operated for two hours and the temperature of the cabinet and transformer did not rise above the limits of safety previously established by the Council. The wavelength was found to be approximately 15 meters. The input power is about 386 watts. So far as it is known, there is no reliable or acceptable method of measuring the output power of short wave diathermy machines.

The machine was tested in a clinic acceptable to the Council and the investigator reported that the unit supplied sufficient energy to heat the body tissues whenever such treatment is indicated. The tissue heating effect in the human thigh was investigated. The technic was that recommended by the manufacturer. Cuff electrodes about 20 inches long and 3 inches wide were used, one wrapped round the thigh proximally to the knee, and the other one close to the hip. When they are applied to the patient, the rubber cuffs are separated from the skin by one-eighth inch felt and one thickness of toweling.

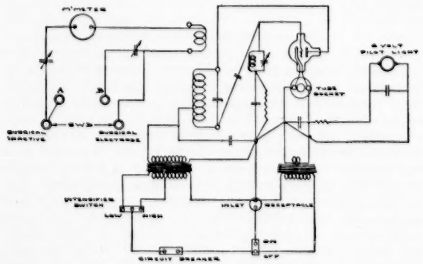

Diagram of circuit.

This technic was used throughout the tests. Thermocouples were introduced into the subcutaneous deep lying tissue (quadriceps extensor).

After twenty minutes' treatment, the machine being operated at the patient's tolerance, the temperature rise (average of seven tests) was observed to be more than that for conventional diathermy using two electrodes, one on the medial and one on the lateral aspect of the thigh.

Electrosurgical investigations were carried out by the investigator in his clinic. The performance and efficacy of the surgical currents generated by this machine were reported to meet the standards expected by the Council.

Burns may be produced by this machine, but with ordinary care they may be avoided; their likelihood to occur is much less than with conventional diathermy.

In view of the foregoing report, the Council on Physical Therapy voted to include the Burdick Short Wave Diathermy Machine (SWD-5) in its list of accepted apparatus.

Council on Pharmacy and Chemistry

PRELIMINARY REPORT OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING PRELIMINARY REPORT. PAUL NICHOLAS LEECH, Secretary.

ACETYL-BETA-METHYLCHOLINE AND MECHOLYL (MECHOLIN)-MERCK

Under the name Mecholin, the firm of Merck & Co., Inc., recently submitted to the Council its brand of acetyl-beta-methylcholine. Subsequently the firm informed the Council that, on account of possible trade mark interference it was obliged to give up the name "Mecholin" and that it would suggest the name "Mecholyl" instead. The question of the firm's right to the use of a proprietary name has not yet received definitive consideration by the Council. Any decision that the Council might reach in this matter would apply as well to the name "Mecholyl" as to the originally proposed name. The Council has voted that the product be not accepted until more extensive clinical studies have been made. In considering this product the Council decided to publish an article on acetyl-beta-methylcholine in the form of the following preliminary statement:

The numerous investigations on acetylcholine have indicated that its action resembles that produced by stimulation of the parasympathetic nervous system but in addition causes dilatation of blood vessels which are not known to be innervated by parasympathetic nerves (limbs, for example). Indeed, there is considerable evidence that acetylcholine is identical with, or at least similar to, the intermediary substance liberated by parasympathetic stimulation, and capable of exerting an action on structures in the body which are distant from the stimulated nerves (Hunt and Taveau,[1] Dale,[2] Loewi,[3] Babkin, Gibbs and Wolff,[4] Gibbs and Szelöczey,[5] Feldberg and Rosenfeld[6]). On the mode of liberation or formation of this intermediary substance in the body, practically nothing is known.

The widespread distribution of choline in the organism has been shown by the many workers who have investigated the problem since Strecker's[7] original isolation of this base from bile in 1849. Since choline is a product of the hydrolysis of phosphatides, it is found wherever lecithins occur.

The demonstration of the presence of free acetylcholine in the tissues is attended by numerous difficulties. Whether appreciable amounts exist in any tissues other than those of the spleen, placenta and adrenal medulla appears, at the present time, exceedingly doubtful (Dale and Dudley,[8] Chang and Gaddum,[9] Minz,[10] Feldberg and Minz[11]). It is of interest that Hunt[12] as early as 1899 discovered choline in adrenal

1. Hunt, Reid, and Taveau, R. DeM.: J. Pharmacol. & Exper. Therap. **1**: 303, 1909-1910.
2. Dale, H. H.: J. Pharmacol. & Exper. Therap. **6**: 147, 1914-1915.
3. Loewi, O., and co-workers: Arch. f. d. ges. Physiol. (1921-1930) **189**: 239; **192**: 201; **203**: 408; **204**: 361; **206**: 135; **208**: 694; **210**: 550; **214**: 678; **217**: 610; **225**: 721.
4. Babkin, B. P.; Gibbs, O. S., and Wolff, H. G.: Arch. f. exper. Path. u. Pharmakol. **168**: 32, 1932.
5. Gibbs, O. S., and Szelöczey, J.: Arch. f. exper. Path. u. Pharmakol. **168**: 64, 1932.
6. Feldberg, W., and Rosenfeld, P.: Arch. f. d. ges. Physiol. **232**: 212, 1933.
7. Strecker, A.: Ann. d. Chem. **70**: 196, 1849; **123**: 353, 1862; **148**: 77, 1868.
8. Dale, H. H., and Dudley, H. W.: J. Physiol. **68**: 97 (Oct.) 1929.
9. Chang, Hsi Chun, and Gaddum, J. H.: J. Physiol. **79**: 225 (Oct. 6) 1933.
10. Minz, B.: Arch. f. exper. Path. u. Pharmakol. **167**: 85, 1932.
11. Feldberg, W., and Minz, B.: Arch. f. d. ges. Physiol. **233**: 657, 1933.
12. Hunt, Reid: Am. J. Physiol. **3**: 18, 1899.

extracts. Shortly after he was able to demonstrate that the extract contained a substance which readily yielded choline on chemical manipulation.[13]

Kapfhammer and Bischoff[14] reported the isolation of considerable amounts of acetylcholine from oxblood, and Vogelfanger[15] and Parnas[16] have confirmed their observations. The work of Dale and Dudley,[17] Dudley,[18] Wrede and Keil,[19] Strack, Neubaur and Geissendörfer,[20] Chang and Gaddum,[9] and Gollwitzer-Meier,[21] however, makes it appear likely that the acetylcholine found by Kapfhammer did not exist as a free substance in the tissues but was formed in the process of the isolation. Strack and his co-workers found that, whereas fresh liver tissue contains practically no free choline or acetylcholine, rapidly increasing amounts of free choline are formed after the circulation is interrupted. They think it not unlikely that the acetylcholine isolated by Kapfhammer arose through the esterification of phosphatides.

PHARMACOLOGY

The pharmacologic actions of acetylcholine comprise two groups: (1) The "muscarine" or "parasympathetic" action and (2) the "nicotine" action. The "muscarine" action is shown by the inhibitory effect on the heart, the vasodilator effect with an accompanying lowering of the blood pressure, and the stimulation of gastric and intestinal peristalsis. All these effects can be prevented or abolished by atropine.

The "nicotine" effects are less conspicuous and are usually masked by the parasympathetic effects unless these are prevented by a preliminary dose of atropine. They are due to stimulation of sympathetic ganglions and result in a considerable rise in the blood pressure. While all derivatives of acetylcholine show essentially the same pharmacologic actions, they do so in varying degree. Hunt and Taveau[22] in 1911 made an extensive study of various compounds of acetylcholine and found that acetyl-beta-methylcholine (trimethyl-beta-acetoxy-propyl-ammonium chloride) possesses marked "parasympathetic" actions and practically no "nicotine" actions. These observations were recently confirmed by Simonart.[23] Menge[24] found that this substance is much less readily hydrolyzed to the less active substance choline than is acetylcholine. Acetyl-beta-methylcholine was first prepared by Taveau[22] and by Menge[25] and was studied pharmacologically by Hunt[26] and by Hunt and Renshaw.[27]

These studies have been extended by a group of workers at the University of Pennsylvania. Comroe and Starr,[28] in a series of experiments on animals, have confirmed Hunt and Taveau's, and Simonart's observations that acetyl-beta-methylcholine possesses practically no "nicotine" action. They compared the duration of the activity of this drug with that of acetylcholine, as observed by Dale,[2] and concluded as had Hunt and Taveau that acetyl-beta-methylcholine is more slowly destroyed in the body. Their data show that the effect on the heart rate and blood pressure lasts for about one minute, whereas the effect on the gastro-intestinal tract often persisted for from ten to twenty minutes. Starr, Elsom, Reisinger and Richards,[29] Abbott[30] and Starr[31] have studied the effects of acetyl-beta-methylcholine in normal persons and in patients with a variety of clinical conditions. In normal subjects the subcutaneous administration of 20 mg. of the drug was followed by prompt and marked effects. Within a minute after the injection, flushing of the face and neck, generalized sweating, salivation, slight fall in blood pressure, and increase in the pulse rate were observed. The effect on the blood pressure and the increase in the pulse rate passed off within a few minutes. This was usually followed by a pulse rate that was slower than before the injection. The other effects lasted for several minutes. In most of the subjects a transient sinus arrhythmia appeared during the period in which the heart was slowed.

In one subject a typical asthmatic attack occurred immediately following the injection of the drug. The authors consider this the only observed reaction that was at all alarming. Three of the twenty subjects experienced a sense of constriction under the sternum. When the drug was administered by mouth, the symptoms were gradual in onset and mild in character. To produce a significant effect by oral administration, between fifty and a hundred times the subcutaneous dosage was required. Intravenous administration was not attempted.

The effects of intravenous injection of acetylcholine in man were recently studied by Carmichael and Fraser.[32] They found that within a few seconds "after injection the heart rate would slow abruptly and simultaneously the subject experienced a sense of obstructed breathing, causing him to cough, or a feeling of constriction in the chest and other minor sensations, such as burning in the throat. Increased rate and depth of breathing was often noticed. The slowing of the heart, the sensation in the throat, and the desire to cough lasted only a few seconds and were followed by a rise of heart rate to a level greater than before injection, by the appearance of a flush over the face and neck, by a sensation of heat throughout the face, trunk and limbs, and in some subjects by palpitation. This second phase passed off gradually and the whole reaction was over in a half to one minute." During the phase of slow heart rate the blood pressure fell but returned to the original level or a little higher during the phase of rapid heart rate. The action of the acetylcholine was found to be increased definitely and prolonged slightly by a previous injection of physostigmine, as Hunt[33] had shown in 1917. In one subject, the injection of 30 mg. of acetylcholine after a previous administration of physostigmine stopped the heart beating for 11.8 seconds, and a convulsive attack followed with auricular fibrillation, which lasted two hours.

CLINICAL STUDIES

The effect of acetyl-beta-methylcholine in the treatment of tachycardia was studied by Starr.[31] Forty-nine attacks of paroxysmal tachycardia were observed. In twenty of these, when pressure over the carotid sinus was the only procedure employed, normal rhythm was reestablished. The other twenty-nine attacks (in nine patients) were treated by the subcutaneous administration of about 30 mg. of the drug, and in a few instances carotid pressure in addition was used. Twenty-four attacks in seven patients were promptly terminated. The patients experienced the same symptoms as did the normal subjects, and after a brief cardiac pause, followed by a period of irregularity of both rhythm and intensity of heart sounds and pulse, normal rhythm occurred. Electrocardiographic observations showed a prolongation of the PR interval and an occasional extrasystole. In two cases this was accompanied by blocked auricular beats and a few aberrant ventricular complexes. This momentary disturbance was followed by normal rhythm. The authors ascribe these effects to vagus stimulation. In one patient, who had been receiving digitalis, a complete heart block was momentarily established, followed by a return of the tachycardia. Whether this was due to any summation of the actions of digitalis and acetyl-beta-methylcholine is uncer-

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33. Hunt, Reid: Am. J. Physiol. **45**: 197 (Feb.) 1918. Hunt and Taveau.[22]

tain. In their experiments on animals, Comroe and Starr were unable to demonstrate such an effect. In preventing the occurrence of attacks, quinidine was found to be much more effective.

In tachycardia accompanying thyroid disease, and in auricular fibrillation, acetyl-beta-methylcholine was without therapeutic effect.

Nahun and Hoff [34] recently reported that acetyl-beta-methylcholine prevents the development of ventricular fibrillation in animals suffering from acute benzene poisoning. These interesting observations await further confirmation.

Starr studied also the effects of the drug in a variety of conditions involving the blood vessels. In Raynaud's disease, acetyl-beta-methylcholine did not prevent or alleviate the spasm when the extremity was exposed to severe cold, but it appeared to have some beneficial effect in spasm following moderate exposure. Only four cases were studied. In four cases of occlusive type of peripheral vascular disease, some relief was noticed in two cases, but it is uncertain whether this can be attributed to the action of the drug. Villaret,[35] who introduced acetylcholine into medicine by using it in the treatment of various types of peripheral vascular disease, considers its use of therapeutic value. Ruiter [36] in 1931 reported therapeutic effects following the use of acetylcholine in the treatment of leg ulcers due to circulatory disturbance, and Waters [37] has observed similar results. However, the number of cases they observed was relatively small, and adequate controls are lacking.

Whereas Villaret [38] believes that the esters of choline which he employed are of some therapeutic value in hypertension, Eldahl [39] observed no beneficial action of acetylcholine in his twelve patients with hypertension and arteriosclerosis. He attributed his failure to the organic changes in the vessels. In patients with hypertension, Starr could demonstrate no definite clinical improvements following the use of the drug. Moderate doses given subcutaneously cause a momentary fall in the blood pressure, during which period the patients were more uncomfortable than before. Oral administration was followed by a decrease in systolic pressure of between 38 to 16 mm. of mercury lasting about thirty minutes. In some of the patients, the drug exhibited no effect on the blood pressure.

The data presented by Starr on the possible clinical improvement in one case each of Cheyne-Stokes breathing, one-sided headaches and Ménière's disease are not sufficiently complete to justify an interpretation of the value of the drug in these conditions.

The action of acetyl-beta-methylcholine on the gastrointestinal tract has been studied by Abbott.[40] While there was an increase in gastric acidity following the use of the drug in two of the nine normal subjects and in three of the six cases of hypochlorhydria, histamine gave a greater response and caused less systemic reaction than did the acetyl-beta-methylcholine. These observations confirm those of Wilkinson,[40] who observed that the effect of acetylcholine on the gastric secretion is uncertain and much less pronounced than that of histamine.

In 1921 Le Heux [41] found that choline increased the peristalsis of the small intestine but that the substance had relatively little effect on the large intestine. Arai [42] a year later reported that with choline he was able to relieve intestinal paresis produced by laparotomy in cats. Kuelhewein [43] made similar observations in intestinal paresis following prolonged chloroform anesthesia. In his normal subjects Abbott found that, when acetyl-beta-methylcholine was administered subcutaneously while the stomach was empty, the effect was a cessation of the normal hunger contractions. When the stomach contained food, the drug increased gastric motility. Oral administration of the drug was observed to increase peristalsis of the small intestine, whereas the effect on the colon was much less certain.

Of the fourteen cases of postoperative abdominal distention treated with acetyl-beta-methylcholine, Abbott reports nine as exhibiting some symptomatic relief. Three cases in which the most favorable results were obtained are reported in some detail. While all three patients undoubtedly had severe abdominal distention, only one showed this condition as a complication immediately following operative procedure.

COMMENT

Acetyl-beta-methylcholine is a drug of considerable pharmacologic interest. Its actions resemble the "parasympathetic" actions of acetylcholine and appear to produce little or no "nicotine" effect. Unlike acetylcholine, it is capable of exerting a physiologic effect when administered orally. When injected subcutaneously its actions appear to be more prolonged than those of acetylcholine, although the effect on the heart rate and blood pressure persists for only a few minutes, whereas with acetylcholine the effect persists for about a minute. The intravenous injection is likely to prove dangerous (Villaret and Justin-Besançon).[44]

In selected cases of paroxysmal tachycardia not responding to the usual therapeutic measures, the careful administration of graded doses of acetyl-beta-methylcholine is probably of value. Overdosage of the drug and administration to patients with asthma should be avoided. For preventing attacks the drug is inferior to quinidine. In other forms of tachycardia and in auricular fibrillation, the usefulness of the drug is not apparent.

The clinical data presented are not sufficiently complete to justify an evaluation of the results obtainable in Raynaud's disease. A larger series of such cases should be observed.

In hypertension the value of the drug appears to be limited to the temporary relief of headache. The discomfort experienced by the patients would constitute a contraindication in most cases.

The therapeutic value of the drug in intestinal paresis following laparotomy should be more definitely established. Unfortunately the evidence presented is insufficient. That the drug increased intestinal peristalsis in normal subjects or in patients with nonsurgical abdominal distention is no indication that the paralyzed intestinal tract of the postoperative patient can be effectively stimulated. These effects of the drug should be studied in a larger series of controlled cases.

The Council cannot at this time accept acetyl-beta-methylcholine (mecholyl Mecholin) until further evidence is available. In the meantime, this preliminary report is issued.

The foregoing preliminary report was sent to Merck & Co. before publication. The firm replied that it hoped publication and consideration of the name could be deferred. Further consideration of the name is deferred for the present. A few minor revisions have been made in the original preliminary report prior to its publication. The Council points out that, since the clinical status of the drug is still experimental, a preliminary informative article should be published; that the report is not derogatory to the product, but the available evidence is not sufficient to justify its acceptance for general use by the profession at this time. The Council commends Merck & Co. for the type of investigation planned or under way, and for its cooperative spirit in dealing with this product. The Council will again consider the product and related questions when further evidence is available.[45]

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45. Since this report was prepared, the following two noteworthy publications on the subject have appeared: the important article on the methylcholines and analogous compounds by Reid Hunt and R. R. Renshaw [37] and a preliminary report by Grace A. Goldsmith (Proc. Staff Meet., Mayo Clin. **9**: 337 [June 6] 1934). Working at the Mayo Clinic she administered acetyl-β-methylcholine orally in doses of from 50 to 1,500 mg. to twenty-nine patients with peripheral vascular disease. In all but a few patients there was a marked rise in the surface temperature of the fingers and toes. In some cases of vascular spasm doses of from 50 to 100 mg. were effective; in patients with organic disease it was necessary to give from 1,000 to 1,500 mg.

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SATURDAY, JULY 27, 1935

BONE MARROW INSUFFICIENCY

The bone marrow is considered today to be an integral organ with many important functions. According to Middleton and Meyer,[1] under normal conditions it is the sole source of the red blood cells, the polymorphonuclear leukocytes and the thrombocytes in adult life. The functioning red bone marrow occupies the entire shafts of the long bones at birth. By the sixteenth year of life, active bone marrow is found in the ends of the long bones, in the flat bones, and in small, spongy bones. The histogenesis of the mature blood cells arising in the marrow is not completely understood. However, it is generally accepted that the root cell or hemoblast is responsible for the development of the polymorphonuclears, the erythrocytes and the platelets. The megakaryocyte of the marrow is believed to be the only source of the thrombocyte; but under disease conditions these large cells may appear in other than myeloid tissue. The delivery of the cellular products of the bone marrow into the circulating blood probably is accomplished by two mechanisms; namely, ameboid movement of the cells and extrusion by growth pressure. The polymorphonuclear elements and the blood platelets migrate from the marrow into the circulating blood by means of their ameboid activity, while growth pressure is the potent factor in delivering erythrocytes into the blood stream. There may be separate stimuli to the production of each type of cell derived from the bone marrow, or the energizing force may be a common one for all types of cells. Hemorrhage stimulates the production of blood platelets. Chemotaxis plays an important part in stimulating the production of leukocytes. While there has been a great advance in the knowledge of erythropoiesis made by the well known work of Minot, Murphy, Peabody, Castle, Whipple and others in recent years, the theory of a constant tempo of red blood cell production still appears sound. Bunting holds that a given quantity of bone marrow can produce erythrocytes only at a given rate and that for an increased production there must occur an extension of the erythrogenic centers.[2] Middleton and Meyer say that, so far as is known, lowered oxygen tension is the only normal stimulus to the extension of the bone marrow.

Insufficiency of the bone marrow may result from primary disease of the myeloid system or from a disease that involves this structure secondarily. In either case the result is some form of anemia or other blood dyscrasia. In patients suffering from aplastic anemia there is an absence or extreme paucity of evidence of regeneration of blood cells. There may be little change in the individual erythrocyte. There is usually leukopenia. The platelets are reduced also, and sooner or later purpuric manifestations complicate the picture of anemia. The cases of aplastic anemia reported usually have followed exposure to the toxic action of arsphenamine, radium, x-rays or benzene. An infection may occasionally lead to total paralysis of the bone marrow. No etiology can be ascribed in some of the cases. The prognosis of idiopathic aplastic anemia is grave, death usually supervening within three months, regardless of the treatment. At necropsy, as would be expected, there is found acellular yellow bone marrow.

Insufficiency of the bone marrow that causes a reduction in the blood platelets may occur from many causes. In cases of essential thrombocytopenia, for example, the most conspicuous feature is the hemorrhagic tendency. According to Minot,[3] 60,000 platelets per cubic millimeter is the level below which bleeding occurs. In the purpura haemorrhagica that attends this condition, bleeding occurs in the skin and mucous membrane with epistaxis, hemoptysis, hematemesis, melena and sometimes hematuria. The clotting time is about normal, but the bleeding time is usually prolonged. Simple measures in hemostasis may stop slight attacks of bleeding; again, transfusions will be effective. No one therapeutic agent has been found to be specific. Such measures have been recommended as vitamins A, B and C, viosterol, iron and calcium, ultraviolet therapy, liver therapy, and dietary measures. When the simpler measures fail, roentgen therapy over the spleen or the removal of that organ has been advised. Splenectomy, however, has not been uniformly successful.

Serious bone marrow insufficiency may also manifest itself in the clinical syndrome of agranulocytosis, in which there is a failure of leukopoiesis. Following depletion of the circulating neutrophils there are prostration, fever, and areas of necrosis usually in the mouth, rectum or vagina. The leukocytes alone are affected in most cases, but there may be an extension

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3. Minot, G. R.: Diminished Blood Platelets and Marrow Insufficiency: A Classification and Differential Diagnosis of Purpura Haemorrhagica, Aplastic Anemia and Allied Conditions, Arch. Int. Med. **19**: 1062 (June) 1917.

of the bone marrow insufficiency producing anemia or a hemorrhagic tendency. The prognosis in agranulocytosis depends largely on the presence of a recognizable cause. Idiopathic neutropenia may undergo remissions, but there is no regularity in their appearance or duration. Middleton and Meyer advise that, by means of appropriate doses of pentnucleotide intramuscularly, every precaution be taken to forestall serious declines in the neutrophils.

Bone marrow insufficiency therefore may manifest itself clinically as aplastic anemia when the marrow fails as a unit, as thrombocytopenia when the blood platelets fail, and as agranulocytosis when there is leukogenic failure.

ACETYL BETA METHYLCHOLINE

For a quarter of a century the cholines have commanded the attention of research workers in medical science. The choline compounds, widely dispersed in nature, have been obtained from many vegetables and organic extracts as well as from certain drugs (especially ergot). The cholines may be considered to be quarternary ammonium bases; they produce two sets of actions: a "muscarine" effect and a "nicotine" effect.[1]

As early as 1914, Hunt and Taveau [2] in an intensive study of cholines reported that one derivative, acetylcholine, was 100,000 times more depressant and only three times more toxic than choline itself. Another derivative in this group that has recently been used in therapeutic trials is acetyl beta methylcholine, described by Taveau [2] in some of his earlier work. Hunt, at the time he was working in the Hygienic Laboratory of the United States Public Health Service, found that Taveau's preparation differed pharmacodynamically from acetylcholine and the other cholines.[2] It had the advantage of being effective when given by mouth. It was more slowly destroyed in the body. It possessed a marked "muscarine" effect and practically no "nicotine" effect. The so-called muscarine effect consists of three actions: an inhibitory effect on the heart, a peripheral vasodilatation with an accompanying fall in blood pressure, and a stimulation of gastric and intestinal peristalsis.

The inhibitory effect on the heart led to the use of acetyl methylcholine by Starr [3] in paroxsymal tachycardia. The results indicate that carefully graded doses are useful in selected cases not responding to other measures. He found it ineffective in other forms of tachycardia and in auricular fibrillation. The occurrence of a peripheral vasodilatation suggested to Starr that this agent might also prove useful in the spastic types of peripheral vascular disease. His clinical trials point to an effectiveness in these cases and also in cases of the occlusive type in which there is some degree of spasm. Eldahl [4] had previously found acetyl methylcholine ineffective in hypertension and arteriosclerosis. He concluded that the presence of organic change in the vessels prevented this action of the drug. Goldsmith [5] subsequently reported a rise in skin temperature in all types of peripheral vascular disease following the administration of acetyl methylcholine. The stimulation of gastric and intestinal peristalsis has led to its trial by Abbott [6] in postoperative abdominal paresis.

Elsewhere in this issue of THE JOURNAL is a preliminary report of the Council on Pharmacy and Chemistry (page 281) reviewing the evidence for acetyl beta methylcholine. The Council declares that it is not warranted at present in accepting the product for inclusion in New and Nonofficial Remedies. The character of research developments under the direction of the manufacturers is commended. The Council points out that the evidence for use of the product in abdominal paresis is inadequate, that its use in peripheral vascular disease needs further study, and that it has a limited usefulness in certain types of tachycardia.

Of further interest is the fact that all the "muscarine" effects may be prevented or abolished by atropine. This action of atropine was attributed by Mueller [7] to a resultant paralysis of the dilator elements. The "nicotine" effect, practically absent in this particular choline, results in a considerable rise in blood pressure. This rise did not usually occur unless the "muscarine" effects had been prevented by previous administration of atropine.

Starr [3] described the clinical response to the subcutaneous injection of 20 mg. of acetyl beta methylcholine. One minute after injection there was flushing of the face and neck, generalized sweating, salivation, a slight fall in blood pressure, and an increase of pulse rate. The blood pressure and pulse rate returned to normal within several minutes. The other symptoms lasted for a brief interval. In most cases there was a transient sinus arrhythmia.

Additional experimental and clinical evidence may prove acetyl beta methylcholine useful in these clinical conditions. In the meantime, the report of the Council on Pharmacy and Chemistry warns that the present status of this drug does not warrant its recommendation as an established therapeutic measure. The intravenous use of the drug is definitely not recommended. It apparently should not be used in allergic patients. Thorough knowledge of its action and caution are necessary if it is to be used at present. Acetyl beta methylcholine, however, is deserving of further clinical trial by those who have the facilities to conduct controlled therapeutic investigations.

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7. Mueller, F.: Arch. f. d. ges. Physiol. **134**: 289, 1910.

Current Comment

THE EVALUATION OF TESTS FOR SYPHILIS IN STATE AND LOCAL LABORATORIES

During the past year the United States Public Health Service in cooperation with the American Society of Clinical Pathologists and participating serologists published the results of a study undertaken to investigate the relative efficiency of complement fixation and flocculation tests as described by serologists in the United States.[1] In determining the relative efficiency of these tests the serologists who originally described the methods were permitted to perform their own tests. The conditions under which the specimens were collected and submitted to the serologists have been published.[2] Since the specimens in the original study were examined by the serologists who had described their own methods, or in their laboratories by other specially trained workers, it is possible that the efficiency of the tests may vary considerably when performed by others not so familiar with the details of the procedure. The Committee on Evaluation of Serodiagnostic Tests for Syphilis proposes during the next few months to furnish samples of blood to state and local laboratories and possibly to a few private laboratories in order that the efficiency of the serologic work in these laboratories may be studied. The conditions under which specimens will be collected and transported will follow those in the original evaluation study. The directors of state and local laboratories who desire to participate in the extension of the evaluation of serodiagnostic tests for syphilis are requested to forward an application immediately to the Surgeon General, U. S. Public Health Service, Washington, D. C., in order that careful consideration may be given to all applicants. Applications should state the name of the serologic test or tests for syphilis employed in the laboratory; if the test has been modified, the extent of the modification should be specified. After all applications have been received, the laboratories will be classified according to the type and modification of serologic tests employed. Specimens will then be sent to selected laboratories performing a given test and to the original serologist who described this test. About 200 specimens from normal presumably nonsyphilitic individuals and 200 specimens from known syphilitic patients will be collected in sufficient quantity to furnish a comparable sample to all laboratories performing a given test as well as to the serologist who originally described this test. A direct comparison between the work of the originator of the test and the work of the technicians in the laboratories performing his test will therefore be possible. From time to time the committee will publish the results of this extended evaluation work, showing the reports of the serologist who originated a test compared with the reports by the laboratories employing his technic. The method followed by the committee in evaluating serodiagnostic tests for syphilis has been indorsed by the American Dermatological Association. The Conference of State and Territorial Health Officers with the United States Public Health Service also passed a resolution during its 1935 meeting approving the method and its extension to include the work in state and local laboratories.

1. Cumming, H. S., Hazen, H. H.; Sanford, A. H.; Senear, F. E.; Simpson, W. M., and Vonderlehr, R. A.: The Evaluation of Serodiagnostic Tests for Syphilis in the United States: Report of Results, Ven. Dis. Inform. **16**: 189 (June) 1935; J. A. M. A. **104**: 2083 (June 8) 1935.

2. Cumming and others: The Evaluation of Serodiagnostic Tests for Syphilis in the United States, Ven. Dis. Inform. **15**: 387 (Dec.) 1934; J. A. M. A. **103**: 1795 (Dec. 1) 1934.

EXPERIMENTAL HYPERTENSION

The introduction of an effective method for the production of experimental hypertension by Goldblatt and his associates[1] has opened a new field in research. Until recently, no method had been available to produce in animals a persistent rise in blood pressure comparable to that which occurs in human beings. By means of an ingenious silver clamp applied to the renal arteries, Goldblatt induced lasting renal ischemia in dogs with resultant increases in systolic blood pressure to from 200 to 240 mm. of mercury; in occasional animals the arterial pressure approached 300 mm. The hypertension lasted indefinitely, often with no detectable change beyond normal limits either in renal function or in the concentrations of urea, total nonprotein nitrogen, creatinine or guanidine in the blood. The condition produced by this means in animals resembles closely that associated with so-called benign nephrosclerosis or so-called malignant nephrosclerosis in man, depending on whether the renal ischemia is moderate or severe. The suggestion has been made that the arterial hypertension associated with disease of the kidney in man may be due to impulses conducted from the kidneys by way of the extrinsic renal nerves to the vasomotor center. Page[2] of the Rockefeller Institute, employing the method of Goldblatt, undertook to test this theory experimentally. He confirmed in detail and extended the observations reported by the latter investigator and his collaborators; he found further that severing the extrinsic renal nerves was without detectable effect on the hypertension induced by renal ischemia. A second method also was employed by Page. This consisted in explanting the kidneys to a position under the skin of the back; after the wound had healed, the kidneys were exposed to roentgen radiation. The rise in blood pressure induced by this means was less severe and of shorter duration than that induced by applying a clamp to the renal artery. With this method also, renal denervation had no effect on the resultant hypertension. Page concludes, "Since the production of arterial hypertension in dogs by constricting the renal arteries, or by irradiation of the kidney with x-ray, is not affected by preliminary stripping of the renal pedicle of its extrinsic nerve supply, these nerves do not appear to participate in the genesis of renal hypertension." Measurements of blood urea nitrogen, plasma protein, total fat, total cholesterol,

1. Goldblatt, Harry; Lynch, J.; Hanzal, R. F., and Summerville, W. W.: Studies in Experimental Hypertension: I. The Production of Persistent Elevation of Systolic Blood Pressure by Means of Renal Ischemia, J. Exper. Med. **59**: 347 (March) 1934. An Investigation Into the Cause of Hypertension, editorial, J. A. M. A. **102**: 1610 (May 12) 1934.

2. Page, I. H.: The Relationship of the Extrinsic Renal Nerves to the Origin of Experimental Hypertension, Am. J. Physiol. **112**: 166 (May) 1935.

lipid amino nitrogen, total lipid nitrogen and phosphatide showed no significant changes following production of renal ischemia by arterial constriction; a slight rise in blood hemoglobin occurred. The solution of various problems in cardiovascular and renal disease has been advanced by means of these new methods of research.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION, PUBLIC HEALTH, ETC.)

ALABAMA

Graduate Courses in Pediatrics.—The Alabama State Medical Association is sponsoring a series of graduate lectures in pediatrics, the first of which will be given some time this summer in cooperation with the Children's Bureau, U. S. Department of Labor. The course will be patterned along the lines of courses in obstetrics which have been conducted in recent years by Dr. James R. McCord, Atlanta, in various states. Dr. T. Cook Smith, assistant professor of pediatrics, University of Louisville School of Medicine, Louisville, Ky., and Dr. John M. Saunders, instructor in pediatrics, Vanderbilt University School of Medicine, Nashville, Tenn., will direct the course, with others assisting.

CALIFORNIA

Plague Infected Ground Squirrel.—A plague infected ground squirrel was shot on a ranch in Lassen County, near Adin, according to the director of the state department of public health, June 24.

Personal.—Dr. Alfred C. Reed, director of the Pacific Institute of Tropical Medicine, University of California, received the doctorate of science at the annual commencement of Pomona College, where he gave an address on "Environmental Medicine."——Dr. Mary B. Ritter, Berkeley, received the honorary degree of doctor of laws recently from the University of California.

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935

ILLINOIS

Hospital News.—A new $100,000 building at the Elgin State Hospital for the Insane collapsed, July 3, injuring seven people. Steel trusses that were being set in the foundation gave way, it was stated.

Committee on Infantile Paralysis.—The appointment of a committee on infantile paralysis is announced by the Illinois State Department of Health, to coordinate all control activities incident to an outbreak of the disease. With Howard J. Shaughnessy, Ph.D., Springfield, the following physicians make up the committee:

Sidney O. Levinson, Chicago.
Philip Lewin, Chicago.
Paul H. Harmon, Chicago.
George W. Staben, Springfield.
Winston H. Tucker, Springfield.
Lloyd L. Arnold, Chicago.
Frank Garm Norbury, Jacksonville.
Frank J. Jirka, director of the state department of health.

Chicago

Annual Golf Tournament.—The Chicago Medical Society will hold its annual golf tournament at the Medinah Country Club, August 7. Those eligible to play are the officers, trustees and past presidents of the society, and members of the council and officers of the branch societies. The trophy is a cup named in honor of the late Dr. J. Warren Van der Slice and donated by Dr. Herman L. Kretschmer in 1933. These tournaments were inaugurated in 1932 by Dr. Austin A. Hayden.

Dr. Hudson Goes to Ohio State.—The appointment of Dr. Noel Paul Hudson, since 1930 professor of bacteriology, University of Chicago, as professor and chairman of the department of bacteriology at Ohio State University School of Medicine, Columbus, is announced. He succeeds Dr. Charles B. Morrey, who has resigned. Dr. Hudson took with him as assistant professors in the department Floyd S. Markham, Ph.D., Jargen M. Birkeland, Ph.D., and Dr. Oram C. Woolpert, all graduates of the University of Chicago. Dr. Hudson graduated from Harvard Medical School in 1925.

IOWA

Death from Rocky Mountain Spotted Fever.—The death of a child, 8 years of age, at Marion, Linn County, June 11, as the result of Rocky Mountain spotted fever, following nine days of illness, is reported in the *Journal* of the Iowa State Medical Society. It is the first case of the disease reported in the state in 1935. A tick was found in the child's scalp, May 31, several days before onset of symptoms, after she had been playing in her front yard.

Society News.—At a meeting of the Davis County Medical Society in Bloomfield, June 25, Drs. Glenn C. Blome and Harold H. Webb, Ottumwa, discussed fractures.——Dr. Everett D. Plass, Iowa City, addressed a joint meeting of the Dickinson and Emmet County medical societies, June 27, in Spirit Lake, on "Diagnosis and Treatment of Leukorrhea."——At a meeting of the Johnson County Medical Society in Iowa City, June 5, Dr. Samuel S. Steinberg spoke on "The Beneficial Effect of High Sodium Chloride Intake in the Treatment of Irradiation Sickness" and Dr. Ernst Freund, "Hypertrophic Arthritis of the Hip."——An illustrated lecture on "Gonorrhea in the Female" was presented before the Washington County Medical Society, June 25, by Dr. William F. Mengert, Iowa City.——Dr. Charles Corbin Yancey, Sioux City, addressed the Sioux County Medical Society, June 20, on "Early Diagnosis of the Adult and Childhood Types of Tuberculosis."

KANSAS

Court Upholds Revocation of Brinkley's License.—The revocation of the license to practice medicine of Dr. John R. Brinkley by the Kansas Board of Medical Registration and Examination was upheld in an order, June 14, issued by U. S. District Judge Tilman D. Johnson, Salt Lake City. Contending that he had been deprived of property without due process of law, Brinkley sought in his action to enjoin the state board from enforcing its order revoking his certificate. The ruling of the judge was a complete endorsement of the board's action in revoking Brinkley's license in 1930. In answering Brinkley's attorneys the judge said, according to the bulletin of the Sedgwick County Medical Society:

> I think that under the general terms of the statute the board is empowered to protect the public against conduct which is clearly against public interest and therefore necessarily unprofessional, the same as if the legislature had specifically denounced and prohibited such practice. Dr. Brinkley's methods were so notorious that ignorance of them by members of the board was an impossibility.
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> . . . It is, I think, perfectly clear from these quotations [from the testimony before the medical board at its hearing] that Brinkley made the practice of medicine a business, adopting usual present-day methods of propaganda by use of mail and radio.
>
> These methods are not only in conflict with ethics of the profession but are in my opinion in conflict with the best interests of the public, and, irrespective of the value of the operations performed by him at the hospital, or the benefits to individuals using prescriptions given through radio broadcasting, the possibilities of injury to the general public resulting from such methods are so apparent that if such methods became general its mere statement is sufficient.

MARYLAND

Tularemia in Baltimore from Tick Bite.—A case of tularemia transmitted by a tick bite was reported in Baltimore early in June. It is the first instance of insect transmission of tularemia to be reported in the state, according to the state department of health, proving that the infection may result not only from handling infected wild rabbits but also from the bites of infected Maryland wood ticks. The patient had not been in contact with rabbits for several months prior to his illness. After he had removed a wood tick that had been engorging for two or three days, an ulcer developed at the site of the tick bite. The patient's lymph glands enlarged; he had fever, headache and muscular pains. Laboratory tests confirmed the diagnosis of tularemia.

MICHIGAN

Memorial to Dr. Warthin.—A bronze plaque of the late Dr. Aldred S. Warthin was presented to the University of Michigan School of Medicine, Ann Arbor, June 15, by persons who had been in the department of pathology when he was director. The memorial hangs in the West Medical Building. Dr. Warthin was associated with the university from his graduation there in 1891 until his death in 1931; since 1903 he had been professor of pathology and director of the pathologic laboratory.

Dr. Parker Honored.—The honorary degree of doctor of science was conferred on Dr. Walter Robert Parker by the University of Michigan at its recent commencement. For twenty-eight years Dr. Parker was professor of ophthalmology at the university; since 1933 he has been professor emeritus.

In 1915 he was chairman of the Section on Ophthalmology of the American Medical Association and, in 1916, he was awarded the Knapp Medal by that section for his research on "The Relation of Tension of Eyeball to Papilledema."

MINNESOTA

State Medical Meeting and Election.—Dr. William W. Will, Bertha, was elected president of the Minnesota State Medical Association at the annual meeting in Minneapolis, June 24-26; he will take office January 1, succeeding Dr. William A. Coventry, Duluth. Drs. Eugene G. McKeown, Pipestone, and Carl W. Rumpf, Faribault, were chosen vice presidents, and Drs. Edward A. Meyerding, St. Paul, and William H. Condit, Minneapolis, were reelected secretary and treasurer, respectively. The next annual meeting will be held in Rochester. The society held joint sessions with the American Association for the Advancement of Science, which was holding its annual meeting in Minneapolis. Guest speakers at the state medical meeting included the following physicians:

Harry L. Alexander, St. Louis, Present Status of Clinical Allergy.
Frank H. Lahey, Boston, Newer Developments in Hyperthyroidism and Hyperparathyroidism.
Edmund Andrews, Chicago, Pathogenesis of Gallbladder Disease.
Theodore L. Squier, Milwaukee, Symposium on Diseases of the Blood: Rôle of Drug Allergy in the Etiology of Primary Granulocytopenia.
Walter A. Bloedorn, Washington, D. C., Rôle of Iron in the Treatment of Anemia.
William P. Murphy, Boston, What We Have Learned About Pernicious Anemia During Ten Years of Treatment with Liver.
Louis W. Sauer, Evanston, Ill., Prevention of Whooping Cough with Bacillus Pertussis Vaccine.
Elmer L. Sevringhaus, Madison, Wis., Endocrine Therapy.
Everett D. Plass, Iowa City, Simplification of Obstetric Care.
John F. Barnhill, Miami Beach, Fla., Suppurations of the Neck: Cause, Diagnosis and Treatment.
William S. Middleton, Madison, Wis., Prognosis and Treatment of Coronary Occlusion.
Thomas G. Orr, Kansas City, Mo., Venoclysis—A Consideration of Its Possible Dangers.

Dr. Murphy addressed a joint meeting of the society with the association for the advancement of science, Monday evening, June 24, on "Diseases of the Blood," and Dr. Percy Brown, Egypt, Mass., delivered the Russell D. Carman Memorial Lecture at an afternoon session, Tuesday, on "The Inception and Development of Fluoroscopy: The Influence of Carman on Its Status in America."

MISSOURI

Dr. Muckenfuss Receives New York Appointment.—Dr. Ralph S. Muckenfuss, assistant professor of medicine, Washington University School of Medicine, St. Louis, has been appointed temporary assistant director of the bureau of laboratories of the New York City Department of Health. Within a few months, the New York *Times* stated, a civil service examination will be held to select a permanent appointee for the position who will be assistant and later successor to Dr. William H. Park, the present director, who will retire on account of the age limit. Dr. Muckenfuss graduated from Emory University School of Medicine, Atlanta, and served for a time on the staff of the Rockefeller Institute for Medical Research, New York.

NEW YORK

Physicians Appointed to Industrial Council.—Governor Lehman has appointed the following physicians to the state industrial council: Drs. William D. Johnson, Batavia; Edward C. Podvin, Horace E. Ayers, New York, and William Linder, Brooklyn. They will represent physicians in their relation to the department of labor in matters concerning the new workmen's compensation law passed by the last legislature. Albert W. Bailey, D.O., Schenectady, was also appointed.

Heads Letchworth Village Twenty-Five Years.—Dr. Charles S. Little, superintendent of Letchworth Village, Thiells, recently celebrated his twenty-fifth year of service at the state institution. Dr. Little went to the colony in 1910 and lived in a tent while the first buildings were being erected, it was said. There are now eleven buildings and two more will be required to finish the building program, which will provide adequate care for 3,650 patients, at a cost of $10,000,000.

New York City

United Hospital Fund to Seek Nine Millions.—A campaign for $9,440,000 will be launched in the fall by the United Hospital Fund, it was announced at a luncheon June 25. Mr. David H. McAlpin Pyle, president of the fund, estimated that this amount would be needed by the fifty-two voluntary hospitals participating in the fund, to stop pyramiding of deficits. Notwithstanding inroads on capital, the hospitals had unpaid bills amounting to $5,700,000 in addition to mortgage and long term liabilities of $14,000,000.

Hearing Tests on School Children.—According to a report of the Emergency Relief Bureau, tests of the hearing of 606,546 school children, made as a special project of the bureau, showed that about 10 per cent had a hearing loss in one ear or both. Of the total number, 4,000 were found to be seriously afflicted and are receiving lip-reading instruction from seventy-nine teachers, who would otherwise be unemployed. The workers were trained in the use of the audiometer at the New York League for the Hard of Hearing, and all children were examined by physicians, who prescribed treatment. Parents who were unable to afford the services of a physician were advised to take their children to clinics, it was said.

Dr. Park to Receive Roosevelt Medal.—Dr. William Hallock Park, director of the bureau of laboratories of the New York City Department of Health, will receive the Roosevelt Medal for 1935, it was announced July 12 by the Roosevelt Memorial Association. The medal will be presented at a banquet at Roosevelt House October 27, the seventy-seventh anniversary of the birth of Theodore Roosevelt. The citation refers to Dr. Park's "distinguished service in the administration of public office." Dr. Park has been director of the health department laboratories since the bureau was established in 1894 and is professor of bacteriology and hygiene at New York University College of Medicine. In recent years he has received the Public Welfare Medal of the National Academy of Sciences and the Sedgwick Medal of the American Public Health Association, of which he was president in 1923. The Roosevelt awards were established in 1923 and are given annually in some field associated with Mr. Roosevelt's career.

OHIO

Dr. Thompson Honored on Hundredth Birthday.—The town of Bethel under the leadership of the local chapter of the Independent Order of Odd Fellows held a community celebration, July 6, in honor of the one hundredth birthday of Dr. William Eberle Thompson. At a public reception Dr. John A. Caldwell, Cincinnati, president of the Ohio State Medical Association, paid tribute to Dr. Thompson's long career and an oil painting of him was unveiled. Dr. Thompson was born in Bethel of a family in which there have been twelve physicians, including his father. He graduated from the old Cincinnati College of Medicine and Surgery in 1860. During the Civil War Dr. Thompson was assigned as surgeon in the Seventh Ohio Infantry. He has had an office throughout all these years on the same street and still conducts a limited practice.

OKLAHOMA

Society News.—Speakers at the quarterly meeting of the Southern Oklahoma Medical Association at Sulphur, June 4, included Drs. Richard M. Burke, Sulphur, on "Differential Diagnosis of Tuberculosis and Nontuberculous Chest Diseases"; John B. Morey, Ada, "Purpura Haemorrhagica," and Anson L. Clark, Oklahoma City, "Fever Therapy—Its Possibilities and Limitations."——At a meeting of the Southeastern Oklahoma Medical Association in Durant, June 27, speakers included Drs. Benjamin B. Kies, McAlester, on "Lymphoid Tissue"; Charles R. Huckabay, Idabel, "Management of Genito-Urinary Diseases by the General Practitioner," and Rufus H. Sherrill, Broken Bow, "Common Complications in Obstetrics."——Dr. William H. Bailey, Oklahoma City, among others, addressed the Woodward County Medical Society at Supply, June 11, on early diagnosis of malignant tumors.

PENNSYLVANIA

Law Enforcement Activities.—The state bureau of enforcement has prosecuted the following persons, among others, in the past few months, for illegal practice of the healing art:

Ashton Will, Somerset, fined $100 and costs with six months imprisonment.
R. D. Singhn, Mechanicsburg, $50 and costs with sixty days in jail.
A. R. Daley, Sharon, fined $100 with six months imprisonment.
Theodore R. Anderson, Philadelphia, one to five years imprisonment.
Eugene Harsch, Pittsburgh, fined $100 and costs.

Philadelphia

Faculty Changes at Jefferson.—During the past session the following promotions and appointments have been made in the faculty of Jefferson Medical College:

Dr. Warren B. Davis, clinical professor of surgery.
Dr. Edward F. Corson, associate professor of dermatology.
Dr. Benjamin P. Weiss, associate professor of neurology.
Drs. Clifford B. Lull, Harry Stuckert and Thaddeus L. Montgomery, assistant professor of obstetrics.
Dr. John T. Farrell Jr., assistant professor of roentgenology.
Dr. Henry B. Decker, assistant professor of dermatology.

TENNESSEE

Personal.—Dr. John W. L. Cooper has been appointed health officer of Chattanooga, to succeed Dr. Frederick C. McIsaac.

Hospital Superintendents Appointed.—Dr. Eugene B. Elder, superintendent of Knoxville General Hospital for about seven years, has been appointed superintendent of Erlanger Hospital, Chattanooga. Dr. Andrew Smith, chief of staff at the Knoxville hospital for the past three years, has been appointed to succeed Dr. Elder as superintendent.

Faculty Changes at Vanderbilt.—The following promotions in the faculty of Vanderbilt University School of Medicine, Nashville, were announced recently, to be effective July 1:

Drs. William R. Cate, Robert C. Derivaux and Hollis E. Johnson, to be associate professors of clinical medicine.
Drs. William Bush Anderson and Milton S. Lewis, associate professors of clinical obstetrics.
Dr. Benjamin H. Robbins, associate professor of pharmacology.
Dr. John M. Lee, associate professor of clinical pediatrics.
Dr. Henry Carroll Smith, associate professor of clinical ophthalmology.
Dr. Edward H. Barksdale, associate professor of urology.
Dr. John S. Cayce, assistant professor of clinical obstetrics.
W. Ray Bryan, Ph.D., assistant professor of physiology.
Dr. Henry L. Douglass, assistant professor of clinical urology.

VIRGINIA

Dr. Broders Appointed Professor.—Dr. Albert C. Broders, Rochester, Minn., has been appointed professor of surgical pathology and director of cancer research at the Medical College of Virginia, Richmond. Dr. Broders is a native of Virginia and a graduate of the Medical College of Virginia. He has been on the staff of the Mayo Clinic for several years.

Society News.—The Warwick County Medical Society held a joint meeting with the Peninsula Dental Society at the James River Country Club, May 14, with Dr. Fletcher D. Woodward, University, as speaker on "The Management of Recent Fractures of the Nose."——A discussion of state medicine, social medicine and compulsory sickness insurance featured a meeting of the Clinch Valley Medical Society at the Lonesome Pine Country Club near Norton, May 24; speakers were Drs. Francis H. Smith, Abingdon, president of the Medical Society of Virginia, Alex F. Robertson Jr., Staunton, and Irl C. Riggin, Richmond, state health officer.

Medical College News.—A portrait of the late Dr. George Paul La Roque, professor and head of the department of clinical surgery at the Medical College of Virginia, Richmond, was presented to the college May 28 by Omega Upsilon Phi and Phi Beta Pi. Dr. William Lowndes Peple made the presentation address and President William T. Sanger accepted the portrait, which will be hung in the college library. Gov. George C. Peery made the principal address at the annual commencement, May 28, at which seventy-six physicians were graduated. Dr. Karl S. Blackwell, Richmond, was elected president of the alumni association.——The medical graduates of 1925 presented to the University of Virginia Department of Medicine at the annual commencement activities, June 8, a portrait of the late Dr. John Staige Davis, professor of medicine from 1900 to 1930. Dr. David R. Lyman, Wallingford, Conn., of the class of 1899, gave the commencement address, June 11, when fifty-four medical graduates received diplomas.

WASHINGTON

State Medical Meeting at Everett.—The forty-sixth annual meeting of the Washington State Medical Association will be held in Everett, August 12-14. A tentative program lists the following guest speakers:

Dr. Olin West, Chicago, Secretary, American Medical Association.
Dr. Edward B. Shaw, San Francisco, Acute Anterior Poliomyelitis.
Dr. Albert H. Rowe, San Francisco, Food Allergy.
Dr. Charles Ulysses Moore, Portland, Ore., Studies in Rickets: Report of 1,000 Cases.
Dr. Herbert W. Riggs, Vancouver, B. C., Pain: Its Relation to Diagnosis.

The program also announces the following addresses by Washington physicians:

Dr. James F. Scott, Yakima, Extraperitoneal Cesarean Section.
Dr. Kenneth K. Sherwood, Kirkland, Prognosis in Chronic Arthritis.
Dr. Arnold W. Hackfield, Seattle, Influence of Modern Psychiatry on Medical Thought.
Dr. Henry H. Skinner, Yakima, Abruptio Placentae.
Dr. Arthur C. Crookall, Seattle, Internal Hemorrhoids: Determination of Method of Treatment.
Dr. Charlton E. Hagyard, Seattle, Acute Pancreatic Neurosis.
Dr. Frank J. Clancy, Seattle, What About State Medicine?
Dr. Walter W. Ebeling, Burlington, Rate of Absorption of Various Fluids by the Bowels.

The Washington State Medical Golf Association tournament will be held Monday, August 12, at the Everett Golf and Country Club, followed by the golfers' annual dinner.

WISCONSIN

Personal.—Dr. William C. Felton was recently appointed health officer of Appleton to succeed Dr. Frank P. Dohearty.——Dr. Amy Louise Hunter, New Haven, Conn., has been appointed supervisor of the state bureau of maternity and child welfare to succeed Dr. Charlotte J. Calvert, who recently retired. Dr. Hunter graduated from Yale University School of Medicine in 1930 and received the degree of doctor of public health at Yale in 1934.

State Society to Collect Historical Material.—Pertinent papers, books and instruments bearing on the history of medicine in Wisconsin are to be collected by the State Medical Society of Wisconsin to form a museum and it is expected that after several years a history of medicine in the state may be written. The State Historical Society has agreed to act as custodian of the material. The *Wisconsin Medical Journal* asks the interest and assistance of physicians in assembling relics and mementos and in preparing articles on individual physicians, institutions, medical practices and the like for publication.

Society News.—Dr. George W. Crile, Cleveland, addressed the Green Bay Academy of Medicine at its annual meeting, recently, on "Surgical Treatment of Polyglandular Disease, Hypertension and Epilepsy."——At a meeting of the Sixth District Medical Society in Oshkosh, June 7, speakers were Drs. Philip W. Brown and Claude F. Dixon, Rochester, Minn., on "Medical and Surgical Treatment of Rectal Carcinoma," and Oscar Lotz, John O. Dieterle and Samuel G. Higgins, all of Milwaukee, on "Diagnosis of Early Tuberculosis," "Use of Kirschner Wire in Maintaining Reduction of Joint Fractures" and "Surgical Care of Eye Injuries," respectively.

Test of Birth Registration.—The bureau of vital statistics of the state board of health recently completed a test on the accuracy of birth registration in all cities in the state with a population of 20,000 or more. It was found that in sixteen cities samples ranging from 11.6 to 25 per cent of the total number of births reported over a period of thirteen years showed 98 per cent completeness of registration. Janesville had 100 per cent registration in 15.3 per cent of all births. The lowest percentage found was 96.8 in Green Bay. In the survey letters were sent to nearly 50,000 couples, whose names were taken from the marriage records in each city. Only couples in which the bridegroom was 30 years old or younger and the bride 25 or younger were considered and only first marriages for both were included. Births reported by the parents were checked against certificates in the state board's files. It was found that the accuracy of registration has increased from 94.6 in 1921 to 98.6 in 1933. Practically all births in Wisconsin are attended by physicians; the percentage increased in the thirteen years from 90.7 to 97.2 per cent, the study showed.

GENERAL

Society News.—The American Dietetic Association will hold its annual meeting in Cleveland, October 28-31. Among speakers will be Drs. Morris Fishbein, Chicago, Editor of THE JOURNAL, on "Food Fads and Fallacies," and Wingate Todd, Cleveland, "Food for Fitness."——The American Psychiatric Association announces removal of its offices to the New York Academy of Medicine, 2 East One Hundred and Third Street, New York.

Association for Study of Goiter.—Dr. Nelson M. Percy, Chicago, was chosen president-elect of the American Association for the Study of Goiter at the annual meeting in Salt Lake City, June 24-26; Dr. Julius R. Yung, Terre Haute, Ind., was installed as president. Among speakers were:

Dr. Robertson Ward, San Francisco, Malignant Goiter—Statistical Survey of Sixty Cases with Comparison of Geographical Types.
Dr. Russell M. Wilder, Rochester, Minn., The Etiology of Hyperparathyroidism.
Dr. George W. Swift, Seattle, Wash., Malignant Exophthalmos.
Dr. Frederick A. Coller, Ann Arbor, Mich., Riedel's Struma.
Dr. Willard O. Thompson, Chicago, Quantitative Observations on the Effect of Iodine in Exophthalmic Goiter in Chicago.
Dr. Arnold Minnig, Denver, Tendency Toward Medical Treatment of Exophthalmic Goiter.

Dr. Wilder addressed a public meeting Monday evening, June 24, on "Prevention and Cure of Goiter." It was voted to hold the next session in Chicago.

Pacific Northwest Medical Meeting.—The fourteenth annual meeting of the Pacific Northwest Medical Association was held in Spokane, Wash., June 27-29. Lecturers were Drs. Fred W. Rankin, Lexington, Ky., who discussed, among other topics, cancer of the breast and of the rectum and selection of gastric and duodenal lesions for surgery; Loyal Davis, Chicago, neurologic surgery; James Edwin Wood Jr., University, Va., rheumatic fever, cardiac edema, pregnancy and hyper-

tension; Tracy B. Mallory, Boston, pathology of asthmatic paroxysms, hyperparathyroidism and pathogenesis of peptic ulcers; Arno B. Luckhardt, Chicago, physiology of the hypophysis and analgesic drugs, and George E. Brown, Rochester, Minn., diseases of the circulation and of the sympathetic nervous system. Dr. Russell T. Congdon, Wenatchee, Wash., was chosen president-elect; Drs. Banner R. Brooke, Portland, Ore., and George O. A. Kellogg, Nampa, Idaho, vice presidents, and Clyde W. Countryman, Spokane, secretary. Dr. Charles T. Sweeney, Medford, Ore., was installed as president. The 1936 meeting will be in Portland.

First Tuberculosis Cottage Rededicated.—In a rededication ceremony during the annual meeting of the National Tuberculosis Association in Saranac Lake, N. Y., June 25, a bronze plaque was placed on "Little Red," the first cottage in America for open air treatment of tuberculosis, erected by Dr. Edward Livingston Trudeau in 1884 in Saranac Lake. The plaque was designed and executed by Mr. A. di Bona, a patient at Trudeau Sanatorium. "Little Red," which is now used as a museum, was recently moved to a new location on the main entrance road to the sanatorium. Using a picture of the cottage on the 1934 Christmas seal, the National Tuberculosis Association commemorated the fiftieth anniversary of the building of the cottage, which was the nucleus of the Trudeau Sanatorium. Dr. Trudeau was the founder and first president of the association. On the eighty-sixth anniversary of his birth, Oct. 5, 1934, officials of the New York state committee on tuberculosis and public health presented to the sanatorium a picture of the cottage in a ceremony attended by physicians from all parts of the state.

Birth and Infant Mortality Rates Rose in 1934.—The Bureau of the Census announces in its annual summary of statistics on live births, infant mortality and stillbirths in the United States that the birth rate in 1934 was 17.1 per thousand of estimated population as compared with 16.6 in 1933. The infant mortality rate for 1934 was 59.9 per thousand live births, as compared with 58.1 in 1933. The stillbirth rate was slightly lower, 3.6 as compared with 3.7 in 1933. New Mexico had the highest birth rate (27.9) as well as the highest infant mortality rate (132.1). States with the next highest birth rates were: North Carolina and Utah, each 24.1; South Carolina, 24; Alabama, 23.4; West Virginia, 23.2, and Mississippi, 23. The lowest rates were in California, 12.7, and New Jersey, 12.9. The highest infant mortality rates after New Mexico were: Arizona, 103; South Carolina, 86.1; Georgia, 78.9, and North Carolina, 77.4. The report points out that the two Western states have large numbers of nomadic Mexicans and Indians and the Southern states large Negro populations. The lowest death rates were those for Oregon, 39.8, and Washington, 43. Mortality rates in several large cities were: New York, 52.1; Chicago, 47.7; Los Angeles, 53.2; Detroit, 50.4; Boston, 57.5; Baltimore, 64.9; New Orleans, 81.5, and Seattle, 41.3. All these rates represent decreases from the figures of 1933 except the last three.

Medical Bills in Congress.—*Change in Status:* H. R. 8554, the Second Deficiency Appropriation Bill, has been reported to the Senate, with amendments (S. Rept. No. 1085). As passed by the House, this bill proposed an appropriation of $20,000,000 to provide additional hospital and domiciliary facilities for veterans. To this sum the Senate Committee on Appropriations added $2,000,000 "to be expended for hospital and domiciliary facilities, subject to the approval of the Federal Board of Hospitalization and the President at the following existing facilities: Newington, Conn., Fort Lyon, Colo., North Little Rock, Ark., and Johnson City, Tenn." *Bills Introduced:* S. 3276, introduced (by request) by Senator La Follette, Wisconsin, and H. R. 8856, introduced by Representative Sauthoff, Wisconsin, propose to pay compensation of not less than $10 monthly to any person totally blind who is or may hereafter become entitled to hospital or domiciliary care under veterans' regulations and, further, to permit such persons to elect to receive monthly the monetary value of hospital care, in lieu thereof. S. 3271, introduced by Senator George, Georgia, proposes, for the purposes of income tax, to permit corporations to deduct charitable and other contributions. H. J. Res. 354, introduced by Representative Wallgren, Washington, proposes to establish a commission to formulate a national policy relative to benefits for veterans and their dependents. H. R. 8849, introduced by Delegate Dimond, Alaska, proposes to construct a hospital for the insane of Alaska. H. R. 8874, introduced (by request) by Representative McSwain, South Carolina, proposes that for the purposes of promotion there shall be credited to officers of the Medical Corps all active service as officers of the Medical Reserve Corps rendered by them between April 23, 1908, and April 6, 1917.

Changes of Status of Licensure.—At a meeting of the Florida State Board of Medical Examiners in Jacksonville, June 17, the following action was taken:

Dr. Albert J. Coleman, Cottondale, license restored.

The New York State Board of Medical Examiners reports the following action:

License of Dr. Julius Phillips, Brooklyn, revoked April 26 following his conviction on a charge of manslaughter by an illegal operation.

The Public Health Council of West Virginia reports the following revocation of licenses, dated March 19:

Dr. William J. Porter, Charleston, and Dr. Clavius Clyde Coffindaffer, Shinnston, for violation of the Harrison Narcotic Law; both are serving sentences in the federal prison at Leavenworth, Kan.

The Texas State Board of Medical Examiners has reported the following action taken at a meeting in June:

Dr. Gustav Raphael Gerson, Houston, license restored, provided he does not apply for a narcotic permit or use narcotics within the next five years.

The Massachusetts Board of Medical Registration recently announced the following action:

Dr. Rafael Reyes Garcia, formerly of Springfield, license restored June 20.

At a meeting of the Arizona State Board of Medical Examiners in April, the following action was taken:

Dr. Richard McClellan Francis, Flagstaff, license revoked following his conviction of a narcotic charge.

Typhoid Epidemic in a Circus—Final Report.—The U. S. Public Health Service has recently published a final report of its investigations of the epidemic of typhoid that occurred in the Ringling Brothers and Barnum and Bailey Circus in the summer of 1934 (THE JOURNAL, Aug. 4, 1934, p. 350). The disease was first recognized in Detroit, where sixty-eight employees were hospitalized July 23 and 24 with symptoms of typhoid. The circus physician asked the help of the Detroit and Michigan state departments of health and because of the interstate operations of the circus the federal health service was invited to participate in the investigation. Nine persons were sent back to Detroit July 25 from Flint, making seventy-seven hospitalized in Detroit, forty-four of whom proved to have typhoid. As the circus proceeded on its schedule, 141 persons were left in hospitals in various cities; seventy-four of them proved to have typhoid. Exhaustive investigation of the personnel for carriers, and of the food and ice supply gave no significant information. Bathing in polluted waters was ruled out. An outbreak of diarrheal enteritis affecting almost the entire personnel occurred July 7-9, when the circus was in western Pennsylvania. Many of those who had typhoid dated their illness back to this outbreak. The typhoid epidemic began about fourteen days after this, the usual incubation period. The distribution among the circus personnel was more or less uniform, all groups being affected except trainmen, porters and elephant men, whose water supply was separate from that of the rest of the circus. Water for the general use of the circus is obtained from city water supplies on contract and it was therefore difficult to account for the fact that the circus personnel became infected while local communities were free from typhoid. Sanitary practices within the circus were found to be extremely crude. Water was usually served in a barrel, keg or bucket equipped with a common dipper or cup. Sewage and garbage disposal were far from efficient, and practically no precautions were taken against flies. Dishwashing was inefficiently done in lukewarm water with insanitary dish towels. Food handlers had not been examined for communicable disease, and their personal cleanliness was far below standard. No effort had been made to require or encourage typhoid inoculations. On recommendation of the health officials, sanitary measures to remedy these conditions were instituted and a physician and a sanitary officer were added to the personnel for the rest of the season to supervise the changes. For future guidance of the circus regimen a set of standard sanitary regulations was drawn up by the federal investigators. The regulations were published in *Public Health Reports*, June 7, 1935, page 797.

LATIN AMERICA

Congress of Physical Therapy.—The first annual meeting of the Latin America Congress of Physical Therapy, X-Ray and Radium will be held in Mexico City, August 29-September 5, with the National University of Mexico as host. Delegates to the congress wishing to present papers will submit the titles of their papers together with an abstract to Dr. Madge C. L. McGuinness, 1211 Madison Avenue, New York, or Dr. Cassius Lopez de Victoria, 1013 Lexington Avenue, New York. The program will be divided into sections representing medicine and

surgery, fractures in their various specialties, electrosurgery, fever therapy, short and ultra-short wave therapy, light therapy, massage, radium and x-ray therapy and exercise. A special nineteen day convention cruise has been arranged with steamer, rail, hotel and sightseeing costs included in one all-expense fee, under the direction of the American Express Company.

Government Services

Positions Open in Children's Bureau

The U. S. Civil Service Commission announces open competitive examinations for several positions in the Children's Bureau, Department of Labor. Applicants must have graduated from a recognized medical school and must have served one year of internship; in addition, certain experience is required. Optional subjects are pediatrics, obstetrics, orthopedics and general practice (maternal and child health). Entrance salaries range from $2,600 to $5,600 a year, less a deduction of 3.5 per cent toward a retirement annuity. Full information may be obtained from the secretary of the U. S. Civil Service Board of Examiners at the postoffice or customhouse in any city which has a postoffice of the first or second class or from the commission at Washington, D. C.

Positions Open for Statisticians

The U. S. Civil Service Commission announces competitive examinations for six positions with the Bureau of the Census, Department of Commerce, two of which are in the division of vital statistics: principal statistician and senior statistician. Applicants for these two positions must have been graduated from medical schools of recognized standing and must have had thorough training in statistics and also in public health, psychiatry or psychology. They must not have reached their fifty-third birthday and must be in sound physical health. Forms for applications, which must be filed not later than July 29 with the Civil Service Commission at Washington, D. C., may be obtained from the commission, from any first class postoffice or from the commission's district offices in Atlanta, Boston, Chicago, Cincinnati, Denver, New Orleans, New York, Philadelphia, Seattle, St. Louis, St. Paul, San Francisco, Honolulu, San Juan, P. R., and Balboa Heights, C. Z. The exact title of the examination desired should be stated in the application form.

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Wellcome Prize Competition

The Wellcome Prize for 1935, a gold medal including a cash prize of $500, will be awarded for the research most valuable for the military service performed in any branch of medicine, surgery or sanitation, *Military Surgeon* announces. Reports of not more than 10,000 words (tabular matter excepted) must be forwarded to the Secretary, Association of Military Surgeons of the United States, Army Medical Museum, Washington, D. C., so as to arrive not later than August 15. Five copies should be sent, signed by a nom de plume or a distinctive device and accompanied by an envelop marked on the outside with the nom de plume and containing the true name of the writer. The winning report will be the property of the association and will be published in *Military Surgeon*. The competition is open to all medical department officers, former such officers, acting assistant and contract surgeons of the army, navy, public health service, organized militia, veterans' administration, U. S. volunteers and the reserves of the United States and all members of the Association of Military Surgeons, except that no person shall be awarded a prize more than once in these contests.

CORRECTION

Dr. Kolmer Has Not Resigned.—Dr. John A. Kolmer, Philadelphia, has not resigned as professor of medicine at Temple University School of Medicine, as reported in THE JOURNAL, July 13, page 127. The chair of medicine is now held jointly by Dr. Kolmer and Dr. Charles Leonard Brown, an arrangement that allows Dr. Kolmer time to conduct research work at the university and at the Research Institute of Cutaneous Medicine.

Foreign Letters

LONDON

(From Our Regular Correspondent)

June 29, 1935.

After the Osteopaths' Fiasco

At a meeting of the council of the British Medical Association Dr. Bone, who presented the report of the osteopathic committee, complained of the large expense incurred by the association, as well as by other professional organizations, in opposing the osteopaths' bill, which went simply to show that no such committee of investigation as was appointed by the house of lords should have been set up at all. He did not know whether there was any redress, but it seemed an inequitable phase of parliamentary procedure. The committee held twelve sittings extending over a period of six weeks and the association, as well as some of the other opposing bodies, was represented by lawyers. Sir William Jowett, the association's attorney, concentrated on clearly defined issues. He made the principal witness for the osteopaths admit that he could not claim state registration without proof of the scientific basis of their claims. He also secured repeated admissions that osteopaths claim to treat all varieties of disease, acute and chronic, that their theory is in conflict with scientific medicine and can give no reasonable explanation of many diseases, and that their theory conflicted with their practice. Before the evidence against the bill could be completed its promoter sounded the retreat, giving the reason that the committee was not competent to try the issue that had been raised as to the want of a scientific basis for osteopathy. This amounts to an admission that the committee should never have been appointed and that the medical bodies which opposed the bill should never have been put to such trouble and expense. But apparently they have no remedy. They must suffer for the want of intelligence of the members of the house of lords who gave the bill a second reading, leading to the appointment of the committee. Before the socialist issue dominated British politics, the reform of the house of lords was a constant demand of many liberal politicians. They ridiculed the hereditary chamber as indefensible. Why should a man legislate because he happened to be the son of a peer? He might be quite unfitted for the task. The fiasco of the osteopaths' bill gives a new point to this argument. It is noteworthy that in the house of commons, which, unlike the house of lords, is an elected and not a hereditary chamber, the attempts of the osteopaths have always failed. Since 1931 four bills were introduced for their registration and were all defeated. The minister of health sensibly took up the position that he could not countenance the registration of an inferior order of medical practitioners and that osteopaths who wanted registration should go through the same course and pass the same examination as physicians.

A point that has come out more strongly since the proceedings terminated is the confounding of osteopathy with bone setting in the press and in the public mind. This has been encouraged by the osteopaths in their desire "to cast the net" as widely as possible. Mr. Blundell Bankhart, an orthopedic surgeon, has stated that he was informed that every one who supported the osteopaths' bill in the house of lords thought that he was voting for bonesetters. Bone setting, he points out in the *Lancet*, is a much older procedure and is British, while osteopathy is American. He might have added that the one is a proper and straightforward procedure (though the competence of its practitioners is in question), while the latter is a fantastic stunt. In a communication to the *British Medical Journal*, Mr. Bankhart states that, while many osteopaths do a certain amount of straightforward manipulation of joints, that

is not osteopathy. Though this divergence from osteopathy in the practice of osteopaths has previously been pointed out, much confusion exists on the subject and was even shown by some of the medical witnesses at the inquiry.

Is Sugar Injurious?

It has been taught for a long time that sugar taken by children in the form of sweets promotes dental caries and also is injurious in other ways. On the other hand, some authorities deny this and consider sugar an excellent food. There seems to be no end to this controversy, which has been revived in the *Times*. Dr. A. C. Jordan, radiologist, who has written a good deal on "intestinal stasis," attacks the practice of giving sweets to children. He declares that they are not sufficiently masticated and therefore not digested by the enzymes of the saliva, and that they pass into "the lower reaches" of the intestine, where they undergo putrefaction and pour poisonous products into the general circulation, impairing the natural resistance of every organ and tissue. These views were vigorously attacked by Sydney W. Cole of the University of Cambridge School of Biochemistry. He points out that cane sugar (sucrose) is not digested by the salivary enzymes, so that no useful purpose would be served by prolonged mastication. Recent radiographic studies show that it passes through the stomach very quickly. It is rapidly absorbed from the blood in the form of dextrose and fructose, a rise in the blood sugar being obtained within ten minutes of taking an ounce. After one has taken as much as 4 ounces, absorption seems to be complete in two hours, while the whole of a pint of raw milk does not leave the stomach in six hours.

Cole also points out that it is impossible for sugar to accumulate in the lower reaches of the intestine, and the lurid picture of it serving there as "a perfect food for pathogenic microbes" is ridiculous. If soluble carbohydrates did exist in the intestine they would be converted by the intestinal bacteria into lactic and other acids, the production of which inhibits the formation of toxins from proteins. In the Cambridge School of Biochemistry Cole teaches, under the direction of his chief, Prof. Sir Gowland Hopkins, that cane sugar is a valuable foodstuff. It is absorbed much more rapidly and with much less digestive effort than an equivalent amount of cooked starch. He also claims that there is no satisfactory evidence that cane sugar is responsible for dental caries or for the increase in the incidence of diabetes. He tells the students that by mouth sucrose is the equal and probably the superior of the more expensive dextrose. He holds that it would be difficult to give a diet of adequate caloric value if sugar, sweets and jams were excluded. All young people engaged in strenuous exercise should have an ample sugar ration. It is well absorbed and has a unique effect in warding off exhaustion. Hence boat crews training on brown sugar do extremely well.

As regards dental caries, the physiologist Prof. Sir Leonard Hill supports the view that sugar promotes caries. It might have been thought that, as sugar is the simplest of all foodstuffs, with a definite chemical constitution, and as it is obtained easily in the pure state, these questions should have been settled long ago.

Loss of Life in the Quetta Earthquake

The loss of life in the Quetta earthquake has been enormous. It is officially stated that the death roll, including the countryside, probably exceeds 40,000. Casualties among people of European birth amount to more than 190 killed and 240 injured. In Quetta itself, out of a population of 45,000, between 20,000 and 30,000 have been killed. The number of destitute refugees is 15,000, of whom many thousands are injured. The public health commissioner, Lieut.-Col. Russell of the Indian Medical Service, is proceeding to investigate the health situation in consultation with the local medical and public health authorities. Some 30,000 Indians and 6,000 Europeans, including troops, have been fed in the refugee camps. Evacuation is still steadily proceeding. Salvage operations were commenced but had to be suspended for hygienic reasons, and in the interests of public health the city remains closed under guard. Only such operations as are consistent with safety and public health are being carried on. The area of the earthquake is estimated at 130 miles long and 20 miles broad. Besides Quetta and the towns of Kalat and Mastung at least 100 villages have been totally destroyed.

PARIS

(From Our Regular Correspondent)

June 14, 1935.

Tuberculosis and Pregnancy

At the March 15 meeting of the Société médicale des hôpitaux of Paris a paper on whether or not pulmonary tuberculosis is influenced by pregnancy was read by Professor Brindeau and his associates, followed by much discussion of the subject, in which leading phthisiologists of Paris took part. During a period of three years 230 cases were followed from a clinical and a roentgenologic point of view. Their conclusions were as follows:

1. A distinct influence on the evolution of a case of pulmonary tuberculosis can be observed only in multiple pregnancies that occur at short intervals in which the child is being nursed, thus weakening the maternal resistance. When tuberculosis shows signs of development during pregnancy, the association of the two conditions is only accidental. The tuberculosis was already incipient and would have developed even though pregnancy had not taken place.

2. One cannot deny the harmful influence of pregnancy on the evolution of tuberculosis. Such a stimulation of the pulmonary lesion is especially to be feared when the latter first presents itself at the beginning of the pregnancy, particularly if the pulmonary lesions are extensive, active and accompanied by febrile reaction. Twelve patients who presented signs of the acute bronchopneumonic type during the first months of pregnancy died. In three fifths of the cases in which there were evidences of the subacute type of tuberculosis at the beginning of pregnancy, death also occurred. In cases in which the lesions had been present for six months before pregnancy began, a fatal outcome occurred in eleven of fifty-four. The harmful influence of pregnancy can be observed even in cases in which there is a slow evolution of the pulmonary lesions. Hence the problem with which one is confronted is to evaluate the intensity of the degree of development and destruction, on the one hand, and the period at which the last acute exacerbation has taken place. This is easy in the acute and subacute forms of recent lesions with cavity formation but is difficult in the chronic fibrous ulcerative forms, necessitating in the last named a visualization of the most recent former evolution and a periodic comparison of the films to determine the date of the last exacerbation as well as the temperature range and a general clinical balance, in order to determine when the next exacerbation is likely to occur. In nine of thirty-six cases there was a recrudescence during pregnancy in the fibrocalcifying type.

3. The harmful influence of pregnancy is most marked during the first three months and during the postpartum period. In the last months the tuberculosis seems to be less active. The latter observations hold true for pregnancy complicated by surgical tuberculous lesions.

In general, one can say that the harmful influence of pregnancy is proportional to the intensity and the length of time the destructive or caseating lesions have existed. The more acute, the worse the outlook. Before interruption of pregnancy is to be considered, every possible measure should be

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employed to control the pulmonary lesions. Twenty-nine patients with subacute evolutive and ulcerative pulmonary lesions treated adequately by artificial pneumothorax were able to be confined at term without perceptible aggravation of the pulmonary lesions. Four out of eleven women in whom the artificial pneumothorax treatment was inadequate died, and seven others required therapeutic abortion. The latter is indicated, first, in recent, evolutive febrile cases in which the tuberculosis is concomitant with the pregnancy, and, secondly, in the dense, diffuse, fibrocaseous chronic type, and finally in cases in which there are ulcerative lesions and an acute exacerbation has occurred during the months immediately preceding the pregnancy.

In the discussion, Professor Sergent stated that every effort should be made to save the life of the mother by therapeutic abortion, when indicated, rather than attempt to deliver at term and lose the mother rather than the fetus. He did not agree with Professor Brindeau when the latter stated that the evolution of the pulmonary lesions at the beginning of the pregnancy was a mere coincidence. In 25 per cent of the cases he has examined, a pregnancy or delivery had preceded by ten months the onset of the pulmonary lesions. The apparent improvement that is observed during the latter months of pregnancy is due to the upward displacement of the diaphragm, thus creating a sort of bilateral artificial pneumothorax.

Danger of Treatment of Epilepsy by Protein Shock

Marinesco and Kreindler of Bucharest reported a case at the March 15 meeting of the Société médicale des hôpitaux of Paris in which treatment by protein shock was applied in a case of severe convulsive attacks. The patient was a girl, aged 18 years. The history of epileptic attacks dated back to the age of 18 months and they had been gradually increasing in frequency, duration and severity. The first injection, of 2 cc. of sterilized milk, was not followed by any reaction. The second injection, of 5 cc., was followed about eight hours later by a series of attacks that were almost continuous. Death occurred thirteen hours after the injection. The temperature before death was 106 F.

The authors maintain that there is a direct relation between the epileptic attacks and the type of anaphylactic shock that follows injection of substances producing anaphylactic shock in animals. Clinically cases have been frequently observed of attacks following the ingestion of cheese, eggs, meat or milk. In certain cases of epilepsy there is a certain pathogenic relation between the attacks and spontaneous or artificially produced anaphylaxis. Bouché and Hustin have observed that frequently the attacks are preceded by vascular phenomena analogous to those seen in anaphylactic shock. Claude, Tinel and Santenoise found that marked lack of balance of the neurovegetative mechanism existed in patients with epilepsy; hence it seems possible that a marked vagotonicity favors the occurrence of an anaphylactic shock. The authors had previously directed attention to the part played by the carotid sinus in the physiopathology of the epileptic seizure, and it seems probable that the anaphylactic shock temporarily influences the excitability of the carotid sinus, thus favoring the appearance of convulsive attacks.

Number of French and Foreign Medical Students in 1935

Dr. Desfosses, editor of the *Presse médicale*, has published statistics on a subject that has caused a great deal of agitation in France. In 1935 there are 10,148 French and 3,021 foreign students in the various medical schools; hence more than a fourth of the total number of 13,169 are foreigners. Ten thousand French students are far more than are necessary to fill the needs for medical men in France and its colonies. Some foreign countries, like Poland, now refuse to allow students to return to their native land to practice, and the same will soon be true of other countries that will not recognize a French diploma. The only method to decrease the plethora in the medical profession lies in the Portmann law, which aims to eliminate students during the first two years who cannot attain a certain grade in their examinations and who have not sufficient preliminary training.

Removal of Thyroid in Cardiac Insufficiency

At the March 27 meeting of the Société nationale de chirurgie, Lian, Welti and Facquet reported three cases of removal of the thyroid in cardiac insufficiency. The cardiologist Lian stated that he had studied the velocity of the circulation in fifty cases of cardiac insufficiency and found the velocity uniformly slower than in normal individuals. His observations confirm those of American investigators to the effect that the circulatory velocity is increased in hyperthyroidism and slower in myxedema. There is a distinct relation between the velocity of the circulation and metabolism. In cardiac insufficiency, Lian has found that the basal metabolism is often above normal; hence the hope to reduce the latter by removal of the thyroid in such patients. In the three cases in which Welti operated, the complete thyroidectomy was followed by a marked improvement of the cardiac condition. The removal of the thyroid was not followed by any evidence of myxedema. In all three cases, medical treatment over a prolonged period had been of no avail. There has been a marked decrease in the dyspnea, in the size of the liver and in a return to normal of the venous pressure as measured with Villaret's apparatus. Operation in the first case was done five months and in the second and third cases three months before being reported. From a technical standpoint, care should be taken not to injure the parathyroids or the recurrent laryngeal nerve in leaving the posterior portion of the capsule.

Committee to Study the Use of the B C G Vaccine

A committee composed of bacteriologists and clinicians, whose chairman is Professor Marfan, has been appointed by the administrative council of the Pasteur Institute. Owing to the fact that several specialists in children's diseases have maintained that the B C G vaccine does not prevent the development of tuberculosis in infants, this committee aims to establish a close cooperation between the institute and those who are occupied in the application of the vaccine.

Masked Forms of Infarct of the Myocardium

Nine cases of the masked form of infarct of the myocardium were reported at the March 5 meeting of the Société médicale des hôpitaux by Laubry and Walser. In its typical form, myocardial infarct is readily recognized by the severe anginal attack accompanied by digestive disturbances, fever, drop in blood pressure and signs of pericardial reaction. Roentgenoscopy and electrocardiography furnish confirmatory evidence but are not essential for the diagnosis. In some cases the pain is the outstanding and only symptom.

In a first group of atypical or "masked" cases, either the pain in the chest was referred to the base of the lung, leading one to think of a pleuropulmonary congestion, or there was pain in the right upper abdominal quadrant, as observed in cholelithiasis. In a second group, there was a complete absence of any pain, and the clinical picture was dominated by symptoms usually considered of lesser importance, such as those of the type of a gastro-intestinal intoxication, of a cardiac collapse, of resistant cardiac insufficiency, or of insular myocarditis with arhythmia of sudden onset. It is not uncommon to find at the necropsy of elderly persons, who have never had anginal attacks, cicatrices indicating myocardial infarcts. The absence of pain depends on the location, rapidity of development and extent of the infarct.

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The masked forms can at times be recognized by a pericardial friction sound. This is a finding of great value from a diagnostic point of view but is seldom present. More constant is a sudden drop in blood pressure. Roentgenography may reveal an aneurysm of the heart, but a great many infarcts are located deeply or on the anterior and posterior surfaces where they cannot be visualized. The electrocardiogram yields more useful information at an earlier period of the condition, but as yet it does not permit localization of the infarct.

BERLIN

(From Our Regular Correspondent)

May 20, 1935.

New Regulations Affecting the Medical Profession

Until recently, ethical questions pertaining to the medical profession were settled by the medical societies or the "chambers of physicians" (aerztekammern). These functions have now been taken over by the Kassenärztliche Vereinigung Deutschlands. Some of the regulations are particularly emphasized. As a rule, no consent to the holding of office hours and to the paying of medical visits in a town in which other physicians are permanently located will be given; nor will consent be given to the holding of regular office hours in a town where there is no physician, or at two separate addresses in a physician's own place of residence. Panel physicians who have been holding special office hours in clinics or hospitals must give them up by July 1, 1935. In a building in which a general practitioner has established a practice, no other general practitioner may open up a practice. The same rule applies to specialists in the same field or in overlapping fields. Seasonal changes in one's place of practice are prohibited. The buying and selling of medical practices is prohibited, but a certain amount by way of compensation for the delivery of a physician's leasehold and equipment, including instruments, may be agreed on, in which transaction the local chairman of the Kassenärztliche Vereinigung must serve as an intermediary. In the future, no consent for the creation of a joint practice, or medical partnership, will be granted. However, the joint use of expensive diagnostic apparatus, such as x-ray apparatus, will be permitted. The age-old designation "general medical practitioner, surgeon and obstetrician," occasionally seen on physicians' signs, must be replaced, before July 1, 1935, by "praktischer Arzt" (general medical practitioner). The designation "praktischer homöopathischer Arzt" (homeopathic general practitioner) may be used only by those physicians who can furnish evidence of adequate training in this field, and who, aside from certain exceptional cases, confine themselves to the homeopathic mode of prescribing. Until the question has been finally regulated, no special designations, such as "biologischer Arzt" (biologic physician) and "Naturarzt" (nature-cure physician) will be permitted. No mention of a physician's hospital practice may be made on a physician's sign. Only the following specialties in medicine are officially recognized: (1) surgery, (2) gynecology and obstetrics, (3) orthopedics, (4) ophthalmology, (5) otorhinolaryngology, (6) dermatology and venereal diseases, (7) urology, (8) neurology and psychiatry, (9) roentgenology and phototherapy, (10) stomatology (for which a license to practice dentistry is necessary), (11) internal medicine, (12) gastrology, enterology and disorders of metabolism, (13) pneumology, (14) pediatrics. Designations of specialists which concern other branches or several of the branches mentioned are prohibited. It is not permissible to combine a designation for a specialty with that of a general practitioner. Likewise the designations "Badearzt" (spa physician) and "praktischer homöopathischer Arzt" are to be considered as referring to general practitioners and hence may not be combined with a title of a specialist. The period of special training for the following specialties is four years: surgery, gynecology and obstetrics, urology, internal medicine; gastrology, enterology and disorders of metabolism; pneumology and pediatrics; for the other specialties the period of special training is three years. Specialists in gastrology, enterology and disorders of metabolism, and also in pneumology, must spend two years of their special training in a department of internal diseases; pediatricians must spend one year in such a department. Candidates for recognition as specialists in urology must furnish proof of three years of clinical activity, in which an opportunity for training in general and urologic surgery was afforded. In addition, a candidate must have had one year's experience in a urologic policlinic or with a specialist in urology. Service in other fields of medicine that are important for a given specialty may be counted up to one year. The training must be obtained at university clinics or in large hospitals of the German reich, or, by way of exception, at a German university clinic or in a large German hospital in a foreign country. The training must be in charge of recognized specialists, and the institution in which it is given must be suitably equipped for thorough and comprehensive special training. The training must extend to all fields of the specialty concerned and hence may not be given exclusively at special centers. Training received in policlinics and in the office practice of recognized specialists must be discounted one half in point of time and can be counted only up to one year at the most. Service in welfare centers and in bureaus of health may not be counted. Approval of a candidate's claims for recognition as a specialist is left to the local chapter of the Kassenärztliche Vereinigung. Such recognition holds good for the whole territory of the reich. Before recognition can be given, candidates must show that they have the necessary special equipment for the practice of their specialty. Specialists must confine themselves, in the main, to their chosen specialty. Specialists who are directors of clinics or of large hospitals or hospital departments must confine themselves, as a rule, to office practice and to consultative activities. Specialists outside this group may make house visits. But they must ascertain whether there is a family physician who commonly treats members of the family, and, in that case, they must insist on a joint visit and must reach an understanding with the family physician in regard to further treatment. The house visits of specialists must by no means take on the form of visits of a family physician, and particularly, other members of the family must not be advised or treated for their various ills. Pediatricians may treat only children under 14 years of age. In private practice, specialists should usually charge higher fees than are charged by general practitioners. A physician serving as a locum tenens of a specialist must be a specialist in the same field as the physician he is representing. These regulations, which go into effect immediately, take away from the Deutscher Aerztevereinsbund many of its most important functions. Even those physicians who do not belong to the Kassenärztliche Vereinigung are, in matters pertaining to professional ethics and to the recognition and conduct of specialists, subject to the decisions of the chairmen of the Vereinigung and must give heed to their instructions.

Congress of Psychotherapy

The specialists in psychotherapy ("seelenheilkunde" is the term now used in Germany) held their congress recently in Nauheim. Some time ago a reorganization of the society according to the racial views of the political party in power was effected, and it is held that psychotherapy, after breaking with the dominant ideas of the past epoch, which claimed Freud as its champion, has not lost its importance. Psychotherapy is not regarded as identical with psychoanalysis as set forth by Freud, and an endeavor is being made, after overcoming the dogmatic psychoanalysis, to create a new "seelen-

heilkunde," or psychotherapy, which will satisfy better the German type of mind. Under the chairmanship of C. G. Jung of Zurich, a number of papers were presented. Zimmer of Heidelberg reported the results of his studies on Indian views concerning psychotherapy. Van der Hoop of Amsterdam presented a paper on "The Personal, the Impersonal and the Hyperpersonal in Psychotherapy." Rümke of Amsterdam spoke on "The Particular Life Phase of the Patient in Connection with Treatment for a Neurosis." He emphasized the idea that psychotherapy is effective only when it considers at the same time what stage of development the patient has reached. From this thought he developed the principle of neuroses, for the various phases of life present widely different demands and every phase has its own peculiar reactions. From this fact result various tasks in connection with the application of psychotherapy, as the physician must take a different stand toward each phase of life and must bear in mind that man's problems vary greatly with each stage of his existence. In dealing with persons who are in the stage of growth and in their best strength, it appears proper to apply psychoanalysis in its complete form. At the turning point of life (age 40-50 years), psychotherapy as outlined by Jung is the sovereign method. In dealing with elderly persons, care should be taken not to insist too fanatically on the patient unburdening his mind completely, as he no longer possesses the elasticity of former days.

Göring of Wuppertal spoke on "The Chances of Success of Psychotherapeutic Treatment." He presented statistics that comprised all patients, over a period of four years, to whom psychologic treatment was applied, organic cases and cases of schizophrenia and manic-depressive insanity having been excluded. The statistics (423 cases) revealed that the prospects of success are worse, the more constitutional factors are involved in a neurosis. On the other hand, more than 70 per cent of successes were attained when there was evidence of a marked influence of environment. With regard to the time necessary for the treatment, Göring found relatively short periods (from three to four months) adequate in most cases. He consistently refused to give treatment extending over several years. Other psychotherapeutists have had about the same experience; but the technic of the specialists varied considerably, since the personality of the physician played an important part.

Another main topic dealt with the teachability of psychotherapeutic science. In this connection it was emphasized that experience in general medicine is desirable and even necessary before practice as a specialist is begun, and that psychotherapeutic training more than any other depends for its success on the individual aptitudes.

Professor Dr. Wilhelm Kolle

The death of Professor Dr. Wilhelm Kolle, who is well known as having been for many years director of the Staatsinstitut für experimentelle Therapie and the associated Georg Speyer-Haus in Frankfort-on-Main, at the age of 66, has been announced. After receiving his training as assistant physician at the Berlin Robert Koch Institute for Infectious Diseases he conducted a scientific expedition in South Africa under the auspices of the government of South Africa, and later an expedition in the Sudan under the commission of the Egyptian government. In 1906 he was summoned to the University of Bern, as ordinarius in hygiene and bacteriology, and became in 1917 the successor of Paul Ehrlich in Frankfort-on-Main. Kolle manifested great pride in the fact that he was a pupil of Robert Koch. In collaboration with R. Pfeiffer, he worked out the bases for immunization against cholera and typhoid, and also performed the first immunizations on man. Collaborating with Wassermann, he established the evaluation of the meningococcus serum and also of the dysentery serum, the plague serum and the arsphenamine preparations. His researches on symptomless syphilis are well known. Kolle was a member of numerous scientific bodies; also a member of the standardization commission of the health committee of the League of Nations. Arsphenamine therapy, the experimental bases of which Kolle had taken over from his predecessor Ehrlich, he developed further in a successful manner.

BUCHAREST

(From Our Regular Correspondent)

June 15, 1935.

Rioting Students Reprimanded

In view of the continuous antisemitic disturbances, chiefly at the faculty of medicine of the university, the universities called a conference with the aim of establishing order. The conference established the fact that the disturbances perpetrated against fellow Jewish students originate partly in the university and student demands, and partly in social and political causes. Formerly the interuniversity council limited the number of students, not on a religious or racial basis but on a basis of individual fitness and competence. A committee was appointed to establish the program of examinations to be passed before enrolment. The official communiqué published in connection with the limitation of the number of students contains the following paragraphs:

1. As an excessive number of students endangers adequate training, the interuniversity council will in the future fix the maximal number of students enrollable four months prior to the opening of the sessions. 2. First year enrolment will be subject to a special examination, the conditions of which will be stabilized by the ministry of instruction and by the board of the universities. 3. Owing to the fact that, in consequence of this measure, the income of the universities will be reduced, the ministry will increase the subsidies due to the universities. 4. The attendance at lectures, seminaries, laboratories and institutes is compulsory for every student. 5. Any student who within two years does not successfully pass the examinations prescribed for one year will be excluded as unfit and will not be enrolled in any of the inland universities.

These measures are intended partly to reduce the number of students and partly to remove students who spend their time in street demonstrations and in politics, thereby neglecting their studies.

Induced Abortion and the New Rumanian Penal Code

The parliamentary committee entrusted with the preparation of the new penal code accepted the following draft: Section 480: Whoever performs or assists in the interruption of the normal course of gestation commits the crime of abortion and is liable to punishment as follows: 1. If the crime is committed without the consent of the woman, the punishment is imprisonment for from three to five years. If the woman succumbs in consequence of the operation, the punishment is from seven to ten years' imprisonment. 2. If an unmarried woman performs the operation on herself or causes the operation to be done by another person, she is liable to punishment of from three to six months in prison; if she is a married woman, the prison term is from six to twelve months. Section 481: The same punishment is due for the attempt of this crime. Section 482: If the operation is performed by a physician, no punishment is due in the following cases: 1. When the pregnancy is the result of criminal violence. 2. If the life of the woman is in danger, as shown by the physician performing the operation and also by another physician prior to the operation. 3. If the pregnant woman was insane, which fact was established also by another physician prior to the operation, and if the legal representative or guardian of the woman gave his consent

in an authentic form. In such cases the physician performing the operation is obliged to make notification of the case within twenty-four hours to the competent magistrate.

The Control of Foreign Graduates

While the proportion of Aryan young men studying abroad is not more than 0.5 per cent, that of Jewish lads is considerably higher. They take refuge in foreign universities. It is not a luxury on their part but rather a restraint. Studying abroad is an expensive undertaking. They have to attend lectures and pass examinations in a foreign language. These young doctors then have to come back to Rumania after graduation, because no European country allows them to practice.

The interuniversity council has adopted the following resolution in regard to foreign diplomas. The notification of diplomas acquired abroad, when there is a reciprocity between the respective country and Rumania, can take place only in those cases in which the permanent public instruction committee established the right of the candidate to study abroad and provided the applicant studied the number of years required in Rumania and passed all examinations required at Rumanian universities. The council, in certain cases, may require the applicant to repeat certain examinations. The application for notification must be sent to the ministry of public instruction, which passes it on to one of the inland universities.

BUENOS AIRES

(From Our Regular Correspondent)

June 10, 1935.

Long Distance Transportation of Blood for Transfusion

A transfusion department was organized by Drs. R. Palazzo and J. Tenconi in the Hospital Italiano of Buenos Aires, more than a year ago, with the aim of supplying preserved blood that can be transported long distances for transfusion. The main reason for establishing the department was to have at hand a stock of cells and plasma already classified for emergencies. The results have been satisfactory. Drs. Palazzo and Tenconi have sent suspensions of erythrocytes in a dextrose solution to colleagues in Rio de Janeiro, Bordeaux and Pavia, in order to prove the possibility of keeping and transporting erythrocytes. Dr. Servantic of Bordeaux performed without any inconvenience transfusions with erythrocytes that had been taken from the blood of persons in Buenos Aires twenty days before. The methods of Drs. Palazzo and Tenconi are based on the studies of Rous.

Antituberculosis Federation

The several separate tuberculosis societies recently merged into one organization, the Federation Against Tuberculosis. The alliance is voluntary, being neither legal nor administrative, and was accomplished by the combined efforts especially of Drs. C. Mainini of the Sociedad de Tisiología of Buenos Aires, G. Araoz Alfaro of the Liga Argentina de la tuberculosis, G. Sayago of the Instituto de Tisiología of the University of Córdoba, A. Raimondi of Buenos Aires and the members of the different beneficient societies and hospitals of the country. The national committee of regional hospitals and asylums voted for the construction of four new tuberculosis sanatoriums simultaneously with the fusion of the antituberculosis centers.

Ventriculography with Iodized Oil

Drs. M. Balado and R. Carrillo of Argentina in an article published in *La semana médica*, March 7, emphasize the diagnostic value of ventriculography with iodized oil. They regard this method as safer than Dandy's encephalography with injections of air and Egas Moniz's arteriography. The latter two methods make difficult the visualization of lesions in the posterior cranial fossa. The authors have performed more than 303 ventriculographies with iodized oil since 1928. In seventy cases of this group they were able to make an anatomic study of the brain post mortem. Ventriculography with iodized oil is, they believe, harmless and permits the visualization of the third and fourth ventricles, the sylvian aqueduct and the foramen of Monro. The authors discuss in detail the technic. They believe that a diagnosis of exact localization of the lesion in the brain can be secured in 90 per cent of the cases by the injection of air and in 100 per cent by ventriculography with iodized oil either by itself or combined with the injection of air.

Special Lectures

Dr. Policard of Lyons, France, delivered lectures on the histophysiology of the lung, silicosis, osteogenesis and spectrography, at the Faculties of Medicine of Buenos Aires, Rosario and Montevideo, during May and June.

Dr. B. A. Houssay has been invited to deliver the Dunham lecture at Harvard, the Hanna lecture at Cleveland, the Harvey lecture at New York and some other lectures at the Academy of Medicine of California and at Stanford University.

Personals

The following appointments have recently been made: Drs. Belou, correspondent member of the Academia Chilena de Ciencias Naturales; M. R. Castex, B. A. Houssay and C. Bonorino Udaondo, honorary members of the Academia de Medicina of Mexico; Arce, Vaccarezza, Bosch Arana and Bonarino Udaondo, honorary members of the Academia de Medicina of Rio de Janeiro; B. A. Houssay, honorary member of the Physiological Society of Great Britain; F. de Paula Miranda of Mexico, A. Turenne of Montevideo and A. Policard of Lyons, corresponding members of the Academia Nacional de Medicina of Buenos Aires. Drs. E. Savino and R. Sammartino were given scholarships from the Guggenheim and Devoto foundations for studies on public health at Harvard, and on cancer in Germany, respectively.

RIO DE JANEIRO

(From Our Regular Correspondent)

June 15, 1935.

São Lourenço Balneary

The São Lourenço Balneary, recently opened in Minas Geraes, is the first of its kind in the South American countries. There are modern installations for bathing in natural gaseous waters, the therapeutic value of which has been demonstrated in several pathologic conditions. There are also showers and departments for massage. São Lourenço Balneary has twenty-four private baths. About thirty persons can take baths in an hour. A physician is the technical director of the balneary.

First Brazilian Congress Against Cancer

At the first Brazilian Congress, organized by the Sociedade de Medicina e Cirurgia of Rio de Janeiro, with the collaboration of the medical societies of the country, at Rio de Janeiro, the official topics will be: In the medicosocial section: (1) mortality from cancer in Brazil, and (2) actual resources for the anticancer crusade. In the clinical section: clinical aspects of precancer (synthesis). In the pathologic section: (1) classification of cancer, and (2) localization and dissemination of cancer in Brazil. The problem of cancer in Brazil will be discussed from several angles. The topics will be presented by two official speakers, one resident at the federal district and the other resident at any of the states of the country, thoroughly discussed by them and then by the attendants to the congress, including those who were previously registered for attendance. The Associação central brasileira de luta contra o cancer will represent, after the congress, the organized body for the crusade against cancer and will have branches in the various states of the country.

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A Home for Needy Brazilian Physicians

The building of the institution La Casa del Médico was recently inaugurated. It was constructed with donations from all Brazilian physicians on a site given by the late Dr. Felicio Torres. It is a three story structure at present but has been built to allow for the construction of five additional floors. The accommodations meet all the requirements for comfort and beauty expected in modern living. Its purpose is to house physicians who are in need of a comfortable home. Those who can pay are given special apartments on the first and second floors. Those who cannot are given apartments on the third floor. There are special wings for old and invalid physicians who can remain there as long as they wish. The Brazilian syndicate of physicians is in charge of the administration of the building. Prominent Brazilian physicians attended the inauguration ceremonies.

Marriages

JOHN R. RODGER, Boyne City, Mich., to Miss Katherine Johnston of Greeneville, Tenn., in New York, July 3.

FLOYD ALTON MCCAMMON, Payne, Ohio, to Miss Ardola May Lechner of Ossian, Ind., May 22.

ELBERT ERVIN MUNGER JR., Spencer, Iowa, to Miss Millicent Christner of Rosamond, Ill., June 29.

RALPH J. THOMPSON to DR. BERTHELLA E. JARVIS, both of Huntington Park, Calif., recently.

JAMES PORTER BAKER JR., to Miss Louise Herbert Rogerson, both of Richmond, Va., June 8.

RALPH F. HELZERMAN, Tecumseh, Mich., to Miss Edna A. Mackenzie of Adrian, June 19.

TOM VANN WILLIS, Brunswick, Ga., to Miss Ouida Jayne Temples of Statesboro, June 8.

SAMUEL R. ZOSS, Cleveland, to Miss Sadye R. Hoffman of Youngstown, Ohio, June 16.

EVERETT C. FOX, Dallas, Texas, to Miss Ella Gertrude Boyce of St. Louis, June 5.

CLYDE O. ANDERSON, St. Petersburg, Fla., to Miss Eileen Masters of Tampa, June 20.

LEON BANACH to Miss Marguerite N. Fitzgerald, both of Jersey City, N. J., June 15.

WILLIAM W. SHORTAL to Miss Minnie Bell Graham, both of Dallas, Texas, June 14.

JUDSON D. DOWLING to Miss Fleta McWhorter, both of Birmingham, Ala., June 8.

HARRY E. BACON to Miss Althea Hildegard Wahle, both of Philadelphia, June 21.

THOMAS OSCAR VINSON, Macon, Ga., to Miss Roesel Stanford of Augusta, June 6.

RAPHAEL J. HENNES, Oxford, Iowa, to Miss Alberta Bauer of Iowa City, April 29.

PHILIP E. BLACKERBY JR., Louisville, Ky., to Miss Clara Mae Hartmetz, June 1.

JOHN H. BOWLES to Miss Mary Joanna Kelsey, both of Muncie, Ind., June 14.

DONALD A. COVALT to DR. NILA GALE KIRKPATRICK, both of Muncie, Ind., recently.

FRANCES M. JOHNSON, Marion, Ind., to Mr. Alyn G. Price of Cleveland, recently.

ROBERT PHELPS BARDEN to Miss Virginia Gates, both of New York, June 15.

ISRAEL ROBERT FRANK, Boston, to Miss Vera Witkin of Brookline, July 17.

HAROLD OYER, Angola, Ind., to Miss Doris Bauer of Fort Wayne, June 7.

VICENTE R. LAZO to Miss Alice Bennett, both of Shelburn, Ind., May 18.

JAMES A. WIGLEY, Mulberry, Ark., to Mrs. Lillian Beneux, May 18.

Deaths

Benjamin S. Warren ✠ Medical Director, U. S. Public Health Service, Chevy Chase, Md.; Tulane University of Louisiana Medical Department, New Orleans, 1891; appointed assistant surgeon in the U. S. Public Health Service in 1900; passed assistant surgeon in 1905, surgeon in 1912, assistant surgeon general in 1918 and medical director in 1930; professor of hygiene, St. Louis University School of Medicine; 1909-1911; sanitary adviser to the U. S. Commission on Industrial Relations, 1913-1915; medical officer of the U. S. Employees Compensation Commission in 1917; author of various government bulletins and articles relating to open air schools, and relation of wages to public health; aged 63; died, May 19, in the U. S. Marine Hospital, Baltimore, of cerebral hemorrhage.

John Westley Wright, Columbus, Ohio; Cincinnati College of Medicine and Surgery, 1873; member of the Ohio State Medical Association and the American Academy of Ophthalmology and Oto-Laryngology; professor of ophthalmology, Ohio Medical University and Starling-Ohio Medical College, 1891-1910; formerly emeritus professor of clinical ophthalmology at the Ohio State University College of Medicine; Civil War veteran; at one time on the staff of the Protestant Hospital, now known as the White Cross Hospital; author of "A Textbook of Ophthalmology"; aged 92; died, May 23.

James Granger Poe ✠ Dallas, Texas; University of Tennessee Medical Department, Nashville, 1894; since 1919 instructor in anesthesia, Baylor University College of Medicine and Dentistry; demonstrator in anatomy at his alma mater, 1895-1896; member of the Associated Anesthetists of the United States and Canada; chief anesthetist to the Baylor Hospital; author of "Modern General Anesthesia"; aged 62; died, June 15, of coronary occlusion.

Paul Colson Perry, Jacksonville, Fla.; College of Physicians and Surgeons, Baltimore, 1897; past president of the Florida Medical Association and the Duval County Medical Society; formerly on the staffs of St. Luke's, Duval County and St. Vincent's hospitals; aged 60; died, June 5, in a hospital at Richmond, Va., of pulmonary embolism, following an operation.

John Port Shaw, Brockton, Mass.; Trinity Medical College, Toronto, Ont., Canada, 1886; member of the Massachusetts Medical Society; for many years on the staff of the Brockton Hospital; aged 76; died, June 5, of myocarditis, arteriosclerosis and nephritis.

Eugene Arthur West, Chicago; Marquette University School of Medicine, Milwaukee, 1913; member of the Illinois State Medical Society; aged 50; on the staff of the Frances Willard Hospital, where he died, June 18, of pulmonary edema and cerebral hemorrhage.

Parker U. Wagoner ✠ Carlisle, Pa.; Temple University School of Medicine, Philadelphia, 1911; past president of the Cumberland County Medical Society; served during the World War; aged 48; on the staff of the Carlisle Hospital where he died, June 14.

Perry Woolery, Bedford, Ind.; Louisville (Ky.) Medical College, 1897; member of the Indiana State Medical Association; past president of the Lawrence County Medical Society; aged 65; died, May 22, of arteriosclerosis and cerebral hemorrhage.

Charles Carr Morrison, Bar Harbor, Maine; Hahnemann Medical College of Philadelphia, 1883; member of the Maine Medical Association; on the staff of the Mount Desert Island Hospital; aged 78; died, May 5, of lobar pneumonia and acute appendicitis.

Julius Niemack ✠ Charles City, Iowa; Georg-August-Universität Medizinische Fakultät, Göttingen, Prussia, 1891; fellow of the American College of Surgeons; surgeon to the Cedar Valley Hospital; aged 75; died, May 5, of cerebral thrombosis.

Asa L. T. Williams ✠ Vandalia, Ill.; Marion-Sims College of Medicine, St. Louis, 1898; president and formerly secretary of the Fayette County Medical Society; on the staff of the Mark Greer Hospital; aged 64; was found dead, June 13.

Joshua Zadok Sexton, Waco, Texas; Vanderbilt University School of Medicine, Nashville, Tenn., 1897; member of the State Medical Association of Texas; aged 63; died, June 3, in a local hospital, of cerebral hemorrhage and hypertension.

Bayard Taylor Mousley, Walpole, N. H.; Baltimore Medical College, 1905; served during the World War; formerly member of the state legislature and school board; health officer of Walpole; aged 56; died, May 30, of coronary thrombosis.

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Thomas A. Wash, Harrodsburg, Ky.; Hospital College of Medicine, Louisville, 1903; member of the Kentucky State Medical Association; mayor of Harrodsburg; aged 56; died, June 12, of chronic myocarditis and arteriosclerosis.

Albert Edward Smethurst, Philadelphia; Medico-Chirurgical College of Philadelphia, 1898; member of the Medical Society of the State of Pennsylvania; aged 63; died, June 12, in the Episcopal Hospital, of coronary thrombosis.

James A. Stevens, Easton, Md.; Jefferson Medical College of Philadelphia, 1882; formerly member of the state board of medical examiners; aged 81; died, June 8, of endarteritis obliterans and gangrene of the left foot.

Charles H. Christian, Fulton, Mo.; St. Louis Medical College, 1890; member of the Missouri State Medical Association; past president of the Callaway County Medical Society; aged 74; died, May 9, of arteriosclerosis.

Martin Luther Bradley, Springfield, Tenn.; Vanderbilt University School of Medicine, Nashville, 1882; member of the Tennessee State Medical Association; aged 75; died, June 26, of chronic valvular heart disease.

John Henry Rice, Hopkinsville, Ky.; Hospital College of Medicine, Louisville, 1904; member of the Kentucky State Medical Association; aged 64; died, June 7, of gangrene of the left hand and anemia.

Alfred W. Pearson, Gold Beach, Ore.; Hahnemann Medical College and Hospital, Chicago, 1888; aged 72; died, April 27, of shock and inanition, following an operation for carcinoma of the bile ducts.

George R. Rohrer ✠ Lancaster, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1880; on the staffs of Lancaster General and St. Joseph's hospitals; aged 81; died recently.

Edward Porter Webb ✠ Crestview, Fla.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1902; past president of the Walton-Okaloosa Counties Medical Society; aged 63; died, May 26.

Elizabeth Matthews, Springfield, Ill.; Woman's Medical College, Chicago, 1890; served with the American Red Cross during the World War; aged 73; died, June 9, of cerebral hemorrhage.

Richard Henry Moers, Houston, Texas; Tulane University of Louisiana Medical Department, New Orleans, 1910; aged 49; died, May 24, in a local hospital, of embolism and coronary thrombosis.

Albert C. Stephens, Barren Springs, Va.; University of Maryland School of Medicine, Baltimore, 1894; member of the Medical Society of Virginia; aged 65; died, May 15, of angina pectoris.

Robert Finney Miller, Brenham, Texas; Tulane University of Louisiana Medical Department, New Orleans, 1893; served during the World War; aged 69; died, April 5, in a local hospital.

Milton Walborn Phillips, Chapman Quarries, Pa.; Medico-Chirurgical College of Philadelphia, 1906; member of the Medical Society of the State of Pennsylvania; aged 65; died, May 28.

Fabian Blanchard, Lindsay, Ont., Canada; University of Toronto Faculty of Medicine, 1893; member of the Associated Anesthetists of the United States and Canada; aged 64; died, May 4.

Mendes Smyle Wechsler ✠ New York; University and Bellevue Hospital Medical College, New York, 1919; aged 39; died, May 25, of acute encephalitis and bronchopneumonia.

Charles Arthur Walter, Glenside, Pa.; Jefferson Medical College of Philadelphia, 1910; member of the Medical Society of the State of Pennsylvania; aged 52; died, April 25.

Marvin Jesse Arthur Miller, Minneapolis; University of Minnesota Medical School, Minneapolis, 1935; aged 24; was accidentally drowned, May 30, in Lawrence Township.

Harry Clemmens Payne ✠ Pella, Iowa; Keokuk Medical College, 1897; president of the Marion County Medical Society; aged 64; died, June 23, of carcinoma of the lung.

Henry G. Maxey, Woodville, Ga.; Georgia College of Eclectic Medicine and Surgery, 1913; aged 43; died, June 14, in a hospital at Atlanta, of furuncle and erysipelas.

Martin John Nolan, Cheyenne, Wyo.; University of Nebraska College of Medicine, Omaha, 1919; aged 41; died, April 11, in Rochester, Minn., of duodenal ulcer.

Simon F. Earnest, Hummelstown, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1891; aged 68; died, May 6, of uremia due to prostatic disease.

George Napoleon Gaboury, Springfield, Mass.; Harvard University Medical School, Boston, 1910; aged 51; died, June 4, of angina pectoris and coronary thrombosis.

John William Patterson, Oconee, Ill.; College of Physicians and Surgeons of Chicago, 1893; aged 67; died, June 7, of abscess of the middle ear and meningitis.

Earle Stanley Prindle, Portland, Ore.; Hahnemann Medical College and Hospital, Chicago, 1893; aged 65; died, May 26, of coronary thrombosis and angina pectoris.

Hugo Gutmann ✠ Schenectady, N. Y.; Medizinische Fakultät der Friedrich-Wilhelms Universität, Berlin, Prussia, 1896; aged 62; died, June 3, of angina pectoris.

Mary J. Whittet, Anchorage, Texas (licensed in Texas under the Act of 1907); member of the State Medical Association of Texas; aged 81; died, May 24.

James A. Lester, Fayetteville, Ga.; Atlanta Medical College, 1894; member of the Medical Association of Georgia; aged 65; died, June 24, of angina pectoris.

William T. Mahon, St. Louis; College of Physicians and Surgeons, Keokuk, Iowa, 1880; formerly mayor of Chamois, Mo.; aged 82; died, May 13, of pyelitis.

Edward Clint Allen, Wayland, Iowa; St. Louis College of Physicians and Surgeons, 1898; member of the Iowa State Medical Society; aged 63; died, May 19.

Leon B. Gordon, Williamsville, Vt.; University of Vermont College of Medicine, Burlington, 1906; aged 59; died, June 10, of cerebral hemorrhage.

Edward Benedict Taylor ✠ Huron, S. D.; Northwestern University Medical School, Chicago, 1894; aged 66; died, June 2, of cerebral hemorrhage.

Robert Arthur Mathew, La Veta, Colo.; Rush Medical College, Chicago, 1897; aged 62; died, May 20, in the La Veta Hospital, of chronic nephritis.

Harry Haynes Rowland ✠ New York; Columbia University College of Physicians and Surgeons, New York, 1903; aged 58; died, May 18.

James Angus Monroe, Wheeling, W. Va.; Eclectic Medical Institute, Cincinnati, 1882; aged 82; died, May 30, of coronary occlusion.

Isaac Singleton Garthwaite, Santa Monica, Calif.; University of Maryland School of Medicine, Baltimore, 1896; aged 70; died, May 18.

Fred Young, Demorest, Ga.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1908; died in April, of cerebral hemorrhage.

Isaac Hale Rathbun, Spring Valley, Ill.; Rush Medical College, Chicago, 1878; aged 84; died, June 11, of carcinoma of the larynx.

Joseph S. Martin, St. Martinsville, La.; Tulane University of Louisiana Medical Department, New Orleans, 1895; aged 62; died, May 15.

George H. Brannon ✠ Manhattan, Ill.; Hospital College of Medicine, Louisville, Ky., 1889; aged 72; died, May 15, of heart disease.

George Chester Pope, San Marino, Calif.; University of the City of New York Medical Department, 1889; aged 73; died, May 4.

Edward A. Schnell, Greenwich, Conn. (licensed in Connecticut in 1893); aged 67; died, June 12, of cerebral hemorrhage.

Paul Jean Woolsey, Kalamazoo, Mich.; Detroit College of Medicine, 1896; aged 69; died, June 21, of carcinoma of the prostate.

Albert J. Fisher, Toronto, Ont., Canada; Queen's University Faculty of Medicine, Kingston, 1887; aged 76; died, May 16.

Edmund Emmet O'Donnell, New York; Yale University School of Medicine, New Haven, Conn., 1898; aged 59; died, May 16.

Ella Batchelder Lefavour Dean, Beverly, Mass.; College of Physicians and Surgeons, Boston, 1920; aged 64; died, May 6.

Charles Albert Mooers, Attleboro, Mass.; New York Homeopathic Medical College, 1876; aged 87; died, April 25.

James D. Weddell, Tyro, Kan.; Washington University School of Medicine, Baltimore, 1872; aged 86; died, in May.

Winifred M. Byrne, San Francisco; California Medical College, San Francisco, 1896; aged 76; died, May 1.

Irvin Sheppard, Sheridan, Ark. (licensed in Arkansas in 1903); aged 67; died, June 16, of encephalitis.

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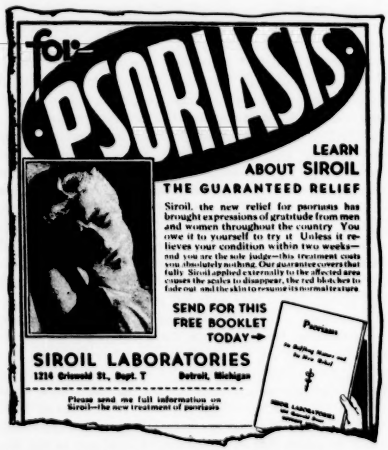
Bureau of Investigation

SIROIL

A "Patent Medicine" for Psoriasis

"Siroil" is a "patent medicine" sold on the mail-order plan by the Siroil Laboratories, Inc., of Detroit. The concern is said to be a Delaware corporation organized in July, 1934. One Ben Kaufmann was reported to have been originally the president of the Siroil Laboratories and to have connected with him two sons, Irvin (who is now president) and Marvin (who is vice president). Among the directors there are said to be Frank V. Martin, Dr. R. J. McClellan and S. Meisner. Mr. Ben Kaufmann is reported to have been in the cleaning and dyeing business for some years and later to have incorporated a jewelry concern that did business on the installment plan, and also to have been vice president of a liquor distributing company. Irvin Kaufmann is reported to have been employed by the jewelry concern already mentioned. Frank V. Martin it appears, is in the advertising business. Dr. McClellan is reported to be a Detroit physician, and Mr. Meisner is said to have formerly been engaged in the retail jewelry business in Columbus, Ohio.


for
PSORIASIS
LEARN
ABOUT SIROIL
THE GUARANTEED RELIEF
Siroil, the new relief for psoriasis has brought expressions of gratitude from men and women throughout the country. You owe it to yourself to try it. Unless it relieves your condition within two weeks—and you are the sole judge—this treatment costs you absolutely nothing. Our guarantee covers that fully. Siroil applied externally to the affected area causes the scales to disappear, the red blotches to fade out and the skin to resume its normal texture.
SEND FOR THIS
FREE BOOKLET
TODAY
SIROIL LABORATORIES
1216 Griswold St., Dept. T
Detroit, Michigan
Please send me full information on Siroil—the new treatment of psoriasis
Psoriasis

According to the advertising, Siroil is "a positive relief for psoriasis." In circular letters sent out by the Siroil Laboratories, signed "I. G. Kaufmann," the sufferer from psoriasis is told: "No matter how difficult or longstanding your case may be, Siroil will give you surprising relief." In advertisements published in the New York *Times* (a newpaper which, before the depression, did not carry "patent medicine" advertising) we read:

> "Siroil applied externally to the affected area causes the scales to disappear, the red blotches to fade out and the skin to resume its normal texture."

Yet the Siroil concern declares that "We are making no extravagant claims for Siroil."

The alleged genesis of Siroil falls into one of the well-known patterns common to "patent medicine" exploitation. The public is told that "an outstanding chemist" who had psoriasis and was "unable to obtain relief from the best skin specialists" began the inevitable "intensive research in an endeavor to find a cure." After six years he is alleged to have developed the preparation which "successfully treated his own condition." Thus was born Siroil.

It is unnecessary to tell physicians that there is probably no skin disease more difficult to treat satisfactorily than psoriasis. The condition is frequently among the most intractable with which the dermatologist is confronted. Yet it is equally well known by medical men that many cases of psoriasis clear up in a remarkable way with treatment. However, the likelihood of recurrence is ever present.

More recently the Siroil concern has brought out two additional products: "Exoil" for eczema and "Siroil Shampoo the Perfect Hair Conditioner."

Because of the number of inquiries that the Bureau of Investigation has received regarding Siroil, the Chemical Laboratory of the American Medical Association was asked to analyze the preparation. The chemists' report follows:

CHEMISTS' REPORT

"Two original bottles of Siroil (Siroil Laboratories, 1214 Griswold St., Detroit, Mich.) were submitted to the A. M. A. Chemical Laboratory for examination. The specimens were not identical in appearance. In general, the preparation appeared to consist for the greater part of a yellow oil together with a small amount of a suspended material which had settled to the bottom of the bottle. No information concerning the composition of Siroil was given by the manufacturer on the label or in the accompanying circular. On shaking, the mixture emulsified; on long standing, a yellow liquid separated and an insoluble material settled to the bottom of the container. When centrifuged, the product separated into two separate liquid layers and a solid. The upper layer was a yellow iridescent oil, indicative of an unbleached mineral oil; the lower layer was a colorless liquid, suggestive of water. The solid material was mostly 'centrifuged' to the bottom of the tube, but some solid substance remained between the two layers. The product had an odor of phenol. The reaction toward moistened litmus paper was alkaline.

"Qualitative tests for heavy metals, such as mercury, salicylic acid, chrysarobin and ammonium compounds were negative. A large amount of mineral oil (suggestive of an unbleached liquid petrolatum) was found; tests also indicated the presence of phenol, sodium chloride (probably as dairy salt), glycerine, water, and a very small amount of saponifiable material, and a small quantity of a waxy substance.

"The specific gravity was found to be 0.894 (approximately 0.9). On heating a specimen for six hours on the steam bath, the loss in weight was approximately 10 per cent. Further investigation indicated approximately 78 per cent liquid mineral oil and the presence of sodium chloride (approximately 0.2 per cent), phenol (approximately 0.15 per cent), a saponifiable material and an insoluble wax-like substance (suggestive of beeswax) approximately 0.25 per cent.

"The foregoing examination indicates that Siroil consists essentially of an unbleached mineral oil roughly 16 parts, water about 3 parts, glycerine approximately ⅕ part, and 1/10 part of each phenol and sodium chloride (salt), and 1/10 part of a saponifiable material and beeswax.

"A preparation having essentially similar properties to those of Siroil may be prepared as follows:

Liquid mineral oil (yellow)	80.0 cc.
Dairy salt	0.5 Gm.
Phenol (crystals)	0.5 Gm.
Glycerine	0.8 cc.
Beeswax (yellow)	0.5 Gm.
Water	17.0 cc.*

* While tests indicated a very small amount of saponifiable matter—probably a fatty oil—it was not deemed worth while to identify the saponifiable matter. Tests indicate that if present, it was in amounts less than one per cent.

"Dissolve the dairy salt and phenol crystals in the glycerine and water; add the mineral oil and beeswax; finally warm and shake."

Reports have come in from persons who have tried Siroil and are enthusiastic about it. On the other hand, a Philadelphia woman writes that after using Siroil "a rash is beginning to appear on my body." A Pennsylvania physician reports that a psoriasis patient of his used Siroil and "developed an eruption on the neck, face and hands characteristic of dermatitis venenata." A Massachusetts physician reports that a patient of his used Siroil "and developed a severe rash wherever it came in contact with her skin."

In other words, the letters to the Bureau of Investigation reflect what one would expect to be the opinions on a preparation of this character: Siroil occasionally helps, occasionally harms, and frequently does neither one nor the other.

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Correspondence

A PROBLEM IN DIETETICS

To the Editor: — Anent the timely article of Alvarez and Hinshaw in THE JOURNAL of June 8 on "Foods That Commonly Disagree with People," may I be allowed to make a comment or two?

I have observed in several of my patients and in my own self that many of the so-called offending foods turn on us, so to speak, because they are not eaten in a state of perfect freshness or after being naturally ripened. This is especially true of the vine-producing vegetables and fruits such as cucumbers and cantaloups.

If such articles are served "fresh from the vine" and not from market shelves, where they may have reposed for hours and days, there will be noticed a total lack of digestive disturbance or at any rate a greatly reduced upset. Doubtless chemical changes take place in such products of the soil after they are separated from the mother stem, and there would seem to be but one moral to draw; viz., "Own your own garden." With modern refrigeration it is a simple problem to have the two "offenders" mentioned thoroughly chilled for fifteen minutes before they are served, and all will be well with the eater.

I have made the same observation regarding the use of sweet corn, for here too its preparation for the table should be expedited after its plucking, just as one would snatch a rainbow trout from the cold, limpid stream and throw it almost writhing on the savoring broiler.

There is no standstill in nature's kingdoms, either vegetable or animal, and it does not hesitate to visit punishment on many an eater of foods that are improperly or insufficiently matured or tardily prepared for consumption. The Englishman may prefer his beefsteak or lamb chop very "high," but he surely flirts with digestive disturbances in so taking it.

Undoubtedly much of the discomfort or distress attending an indulgence in shell-fish is primarily due to the fact that toxins develop during the period following its removal from native haunts to the hour of its consumption. It would seem to me that the chemistry of many foods will yet bear closer study regardless of their content in vitamins.

Why does the lowly onion "in the raw" so frequently retrace its course upward from stomach to palate, whereas, if eaten after floating on waves of acetic acid or after a thorough steaming and delicious creaming, it stays "put." Chemical and physical changes, both gross and fine! Similarly, and yet paradoxically, on the contrary raw cabbage versus boiled cabbage. Again, compare the result of eating under-ripened fruits, such as the highly thought of banana, with that following the partaking of the same fruit thoroughly ripened on the tree. Similarly with the citrus family.

These points may be looked on as unpractical, but they must be taken into account in any logical discussion of dietetics.

When one stops to consider the excellent quality of milk as a culture medium, is it to be wondered at that so many individuals apparently in normal or average health complain of this food in their diets? What though the bacterial count is low at the laboratory or that pasteurization has been done, what is really known as to the changes that have taken place from the time of its withdrawal from the giver until it is consumed? There is nothing to govern one's decision as to its fitness for use except the taste of it, and this may be far misleading.

The same observation must be equally true of so unstable a product as the altogether worthy egg, which when "gathered" from the still warm nest of the cackling biddy is food fit for the gods.

I recognize in this discussion a factor known as allergy so far as the protein content of foods is concerned, but I believe that the term is being used to cover a big bit of ignorance regarding the composition of a strictly fresh or naturally ripened food as compared with that of the same food kept for varying periods either in cold storage or at ordinary temperatures, or brought to the consumer through an artificial process of ripening. It may be that in this instance as in many others "our greatest assets will prove to be the things we do not know."

Practically speaking, what we as physicians need to do in formulating diets for our patients is to guide the individual along sane lines of thought not only as to food values but as to the advantage of procuring foods as fresh or as naturally matured as posssible and of serving them as best befits the individual, for it may still be true that "what is one man's food may be another's poison."

MAURICE B. BONTA, M.D., Los Angeles.

ANAPHYLAXIS AND ANESTHESIA

To the Editor:—It has come to my attention that an answer to a question on the effect of a general anesthetic on anaphylactic shock appearing in THE JOURNAL, Oct. 1, 1932, page 1194, has been referred to in medical teaching as implying "that a general anesthetic is likely to prevent or at least delay anaphylactic shock, if, during anesthesia, foreign protein is injected in a sensitized patient," Although this answer includes the caution that its apparently favorable effect should not be allowed to displace other precautionary measures, nevertheless I believe it goes too far when it implies that general anesthesia is of any aid. The literature on anyphylaxis is generally opposed to such a view. The apparent origin of the opinion that anesthesia would prevent or alleviate anaphylactic shock was Besredka's report that ether narcosis would prevent anaphylactic shock in guinea-pigs, This was not confirmed by Anderson and Rosenau in their early work and has failed of confirmation by other workers. Bally (*J. Immunol.* **17**:223 [Sept.] 1929) has shown that ether anesthesia does not deter anaphylactic shock in the rabbit. Kraíka, McCrea and Vogt (*J. Physiol.* **68**:292 [Nov.] 1929) have obtained anaphylactic shock in cats under anesthesia. The great majority of the work on anaphylaxis in the dog has been done under anesthesia of various kinds. The nature of the anesthetic used has not been mentioned in many instances apparently because of the writer's conviction that it was generally known that anesthesia would not vitiate the results. Weil, however (*J. Immunol.* **2**:525 [Oct.] 1917), saw fit to comment as follows: "Parenthetically it should be added that ether anesthesia does not in the least inhibit acute anaphylactic shock with death in dogs." Manwaring and his collaborators in numerous papers, Simonds, Voegtlin and Bernheim, Heymans and many others have reported work in which various anesthetics were used without preventing shock. In the dog, my associates and I have used ether, chloroform, paraldehyde, barbital and vinethene, with and without morphine, and often in combination, without any apparent ameliorating effect. To be sure, vomiting is prevented in the dog by anesthesia and perhaps the bronchial constriction in the guinea-pig may be somewhat less intense, but there is no substantial evidence that if sensitization is high the fatal issue has been either postponed or prevented. I know of no adequately controlled observations in man that warrant a conclusion of any sort. However, the experiments on laboratory animals but partially referred to here, together with the evidence that anaphylactic shock is largely a histamine intoxication (Gebauer-Fuelnegg and Dragstedt, *Am. J. Physiol.* **102**:520 [Nov.] 1932) and that ether anesthesia (Dale, *Brit. J. Exper. Path.* **1**:103 [April] 1920) increases the susceptibility to histamine not only lend no support to the idea that anesthesia would diminish anaphylactic shock but actually indicate the reverse.

CARL A. DRAGSTEDT, M.D., Chicago.

Queries and Minor Notes

ANONYMOUS COMMUNICATIONS and queries on postal cards will not be noticed. Every letter must contain the writer's name and address, but these will be omitted, on request.

OPTIMUM AIR CONDITIONS

To the Editor:—A man, aged 55, who has an old fibrous tuberculosis of the left lung, now inactive, has had his office air conditioned. What is the optimum humidity for him? What the temperature in relationship to the outside air?

W. P. ADAMSON, M.D., Tampa, Fla.

ANSWER.—The human body functions best in a temperature of from 68 to 70 F. with a relative humidity of from 40 to 50 per cent. However, the factor of safety is such that no great harm comes from somewhat higher or lower temperatures and corresponding changes in humidity.

There is no good evidence to prove that humidity has any significant influence on old fibrous tuberculosis. At one time it was believed that the râles indicating moisture, which one often elicits over an area of progressive tuberculosis, could be influenced by reducing the humidity of the air. More logical thinking, however, convinces one that the moisture elicited over the area of disease is produced in and about the pathologic process rather than by the outside air that one inhales. A tuberculous process is often spoken of as becoming dry. By this it is meant that less evidence of moisture is elicited on physical examination and that there is decrease in expectoration. If the tuberculosis is of the chronic type, there is evidence of fibrous tissue deposits. Here again the deposition of fibrous tissue is not dependent on presence or absence of moisture in the air that one inhales but on the proliferation of connective tissue cells. One sees persons who develop clinical tuberculosis while working in places where the air is extremely dry and yet moist râles may be elicited over the lesion. Again, one sees patients whose lesions show marked decrease in moisture and the deposit of much fibrous tissue while they are being treated in very humid air. It appears, therefore, that the air one inhales, so far as its humidity is concerned, has but little to do with the progressiveness or retrogressiveness of the tuberculous process. Therefore, air conditioning is a matter of providing air free from dust contamination, with the temperature and relative humidity in which the body not only is most comfortable but also functions best.

In the winter it is customary to heat houses and buildings where people work to approximately 70 degrees, although the outside temperature is freezing or below. This has proved satisfactory. Therefore it is just as logical during the summer months to cool the air in buildings to approximately 70 degrees when the outside temperature is high. For a patient with an old fibrous tuberculosis that is inactive, an attempt through air conditioning to keep the temperature of his office at approximately 70 degrees and the relative humidity at 40 to 50 per cent should not only add much to his comfort but also contribute to his health.

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RECURRENT SWELLINGS

To the Editor:—A man, aged 61, has had recurrent swellings of the face, throat, tongue, hands and feet for four years. The swellings almost always come on at 3 o'clock in the morning and apparently involve the tissues deep to the skin, although there may be some slight swelling and irritation of the skin but not accompanied by urticaria. The first attack apparently dated from an attack of jaundice, which lasted about three months and according to the history was suggestive of catarrhal jaundice. These have recurred every one to three weeks since and swellings as large as a hen's egg are somewhat relieved by epinephrine hypodermically. Investigation has revealed no sensitivity to common foods. The patient's blood calcium is normal and he has had no history of asthma or hay fever and has not been benefited by the administration of calcium. He has also had his teeth removed without benefit. At present I am giving him three-eighths grain (0.025 Gm.) of ephedrine at bedtime with the idea of warding off the attacks. What further investigation or treatment would you suggest? Please omit name.

M.D., Ontario.

ANSWER.—The cause of the swellings is problematic. The fact that they occur at 3 o'clock in the morning would indicate that something taken just before bedtime, either a food or a drug, may be the cause; or the patient may be hypersensitive to some article in the bedroom, such as a horsehair mattress, a feather pillow or a camel hair blanket.

It is suggested that, if any of these are present in the bedding, they be removed and then if symptoms clear up that they be brought back one at a time to see if the swellings recur.

Drugs are a common cause of swellings, especially drugs containing quinine or coal-tar derivatives such as acetylsalicylic acid, amidopyrine and acetanilid. These are often taken not only in the form mentioned but also frequently combined in proprietary and "patent" medicines. There are many cases of idiosyncrasies to certain sleeping medicines, such as barbital preparations; some of these contain coal-tar derivatives and barbital. Occasional cases have also been reported from the use of ephedrine, even though ephedrine is used with the idea of combating attacks.

It is suggested also that a food diary be kept, especially of the evening and night meals, and that the foods which are commonly eaten at those times be omitted one at a time for a period of about one week to see what effect will follow, if any.

If skin tests were completely carried out, they need not be repeated; but, if the tests were incompletely done, information may be obtained by such methods in many cases.

MEDLAR'S RATIO FOR LEUKOCYTES IN TUBERCULOSIS

To the Editor:—Can you give me any information about Medlar's ratio as mentioned herewith: "The leukocyte count affords us a method of obtaining a biopsy, so to speak, which mirrors the pathological tuberculous process and thus gives valuable prognostic information. In Medlar's interpretation the polymorphonuclear, the lymphocyte and the monocyte are all concerned in the pathological processes at some time during the infection. Some investigators favor the polylymph ratio, others the monocyte-lymph ratio. Recently a slide rule has been devised by which Medlar's pathological conception, based on the leukocyte count, can be expressed in the form of an index. While the Schilling count is of distinct value, yet considering the extra time, the skill required in differentiating the cells, and the possibility of error, it is our belief that, with the possible exception of the acute tuberculous process, it does not give added information that cannot be obtained from Medlar's formula."

G. WARD DISBROW, M.D., Summit, N. J.

ANSWER.—Medlar has published in the *American Review of Tuberculosis* (**20**:312 [Sept.] 1929) a study of the leukocytic reaction in the blood in tuberculosis. He performed weekly total and differential leukocyte counts in 120 cases. In all the charts 5,000 neutrophils, 2,000 lymphocytes and 700 mononuclears were used as the base lines.

The mononuclear leukocyte (the epithelioid cell of the tubercle being the mononuclear leukocyte of the circulation) forms the primary tubercle and takes a large part in the repair of the tuberculous lesion following caseation. The neutrophil is the chief cell in the formation of tuberculous abscesses that leave cavities and ulcers. As long as these continue to enlarge, the neutrophils are increased. The lymphocyte appears in the process as the predominant cell only when the lesion (primary tubercle, caseous lesion or ulcerated lesion) is in the healing stage. The lymphocyte remains in the healing or healed area long after the other leukocytes have ceased to play a part.

From the leukocytic graphs, made from the numbers of each of these three types of cells found in the blood, certain conclusions can be drawn regarding the progress of the disease in each case. The leukocytes respond to the type of damage done to the tissue. In general, the mononuclear leukocyte increase indicates new tubercle formation, the neutrophil tuberculous abscess formation, and the lymphocyte healing of the tuberculous process.

In the majority of cases there is a close agreement between the clinical progress of the case and the leukocytic interpretation. The leukocytes are often the first indication of an exacerbation, even before the appearance of clinical symptoms or x-ray evidence. The majority of tuberculous cases present a stable leukocytic picture. Patients with a septic leukocytic picture are liable to have hemorrhages or exacerbations. Patients with a high lymphocyte, low neutrophil count and only slight mononuclear increase do not have hemorrhages or serious spread with such a leukocyte picture. A lowering of the neutrophils and mononuclears, with rise of the lymphocytes, indicates a tendency toward healing.

There are three types of leukocytic formulas indicative of three phases of tuberculosis. These types may shift from one to another with changes in the disease process:

1. In the septic leukocytic picture the total count is usually above normal. The neutrophils are above 65 per cent, usually 70 or more. The lymphocytes are never above 25 per cent and usually below 20. The mononuclears are usually above 8 per cent and may be as low as 5 per cent. This type indicates that the lung process is undergoing abscess formation or extension. Healing is not taking place. A mononuclear count above 9 per cent speaks for new tubercle formation.

2. In the hyperplastic picture the total white count is usually within normal limits, never greatly increased. The mononuclears are above 10 per cent, the neutrophils below 60 per cent, the lymphocytes 25 per cent or more. This indicates new tubercle formation, but without abscesses. With lymphocytes above 30 per cent there is a tendency toward healing.

3. In the nonseptic picture the total count is not over 10,000. The percentage of lymphocytes is high, approaching closely the neutrophil percentage. There may even be more lymphocytes than neutrophils. The mononuclears are below 10 per cent. This picture indicates healing, with no abscess formation and but little indication of new tubercle formation.

Flinn has recently concluded that a high monocytic count, with a normal or low lymphocytic count, suggests an active proliferative lesion. A rising monocyte count suggests an extension or exacerbation of the proliferative process or a complicating extrapulmonary lesion. A high neutrophil percentage suggests an exudative lesion. A rising neutrophil percentage suggests extension or exacerbation of the exudative process. A high lymphocyte count suggests an increased tendency to heal.

The blood picture, therefore, may give valuable aid in determining the kind of changes occurring in the tissues. The leukocytic reaction often agrees closely with the clinical status at the time the blood is taken. Blood counts at frequent intervals are of real value in determining the trend of a case of tuberculosis. The blood picture may reveal an extension of a lung lesion before the physical or roentgenographic signs.

HAY FEVER

To the Editor:—A boy, aged 10 years, has always been delicate, is growing fast, is about 2 inches over the average height and is about 2 pounds under the average weight. He has always been active and more energetic than most boys of that age. Large adenoids had to be removed at 2 years of age, the tonsils at 3, the appendix at 6; he had whooping cough at 2 years, measles at 5 and chickenpox at 8. When he was 4 years old he was exposed to poliomyelitis and was given one dose of antipoliomyelitis serum. Within half an hour he was covered from the top of his head to the soles of his feet with an urticaria. There was absence of vomiting or other symptoms. This condition lasted ten days and was controlled with maximum doses of epinephrine and ephedrine with atropine. Last January a slight attack of influenza lasted three days, but following that there was a slight elevation of temperature, less than 1 degree, during some part of the afternoon, lasting two months, during which time he was kept strictly at rest. Nothing could be found in the lungs, sinuses, teeth, abdomen or ears to account for it. Roentgen examination of the chest and abdomen proved to be negative, as also were four tuberculin tests with old and new tuberculin. About three weeks before this was written, some congestion of the eyes and nose developed which tended to clear up and was made much worse one day when he picked a few dandelions. This was very suggestive and skin tests were made. It was found that he was sensitive to a great many of the foods, including milk, eggs and cereals, and to almost all the pollens usual for this district, including dandelions, which was very marked. No basal tests have been made, but all the blood counts have been practically normal. The kidneys have always been normal, except that at 5 years he had a slight pyelitis; but frequent examination since then has never shown any pus cells or abnormality. At the present time the only symptom is some congestion of the turbinates, with some obstruction of breathing, especially during the night. I would appreciate knowing if there is anything that can be done for this generalized allergy to both foods and pollens. No foci of infection have been found anywhere in repeated examinations. Please omit name and address.

M.D., Canada.

ANSWER.—The fact that congestion of the eyes and nose occurred about three weeks before the query was written coincides with the beginning of hay fever due to grass pollen. If this is correct, and the positive skin tests would seem to confirm this, the symptoms will continue until the grass pollen season is at an end, somewhere about the first of August.

If, in addition, the boy is hypersensitive to ragweed, the hay fever will start up again about the middle of August and carry on until the first frost.

The picking of the dandelions and the positive skin test to dandelions signifies little, as dandelion pollen is carried little by the wind and therefore is not important as a cause of hay fever.

The child should receive coseasonal injections, small doses, intracutaneously, at this time of dilute grass pollen extract; e. g., 1:10,000. The first dose might well be 0.1 cc. and this dose should be repeated every day or every other day for a week or two and then gradually increased until August 1. This procedure might clear up the condition promptly. All foods that gave positive skin tests should also be thoroughly eliminated from the diet, at least during the hay fever season, and if they cause symptoms at other times of the year they should also be avoided. However, before it is concluded that the boy is clinically sensitive to these foods, such as milk, eggs and cereals, he should be tested out at some future time outside of the pollen season by removing the foods and then prescribing them to see whether symptoms result.

Clinical sensitivity and positive skin tests are not synonymous by any means. Many patients have given positive skin tests to certain foods but may eat these foods with impunity. On the other hand, many individuals with negative skin tests cannot tolerate certain foods. In other words, every positive skin test, either to proteins or to pollens, must be corroborated clinically before definite conclusions can be reached.

In addition, the fact that the boy gave a reaction to serum suggests extreme caution in receiving any further doses of any kind of serum if this should be necessary at some time in the future. Such serum should be administered very slowly and in many divided doses.

PAROXYSMAL TACHYCARDIA

To the Editor:—A man, aged 51, an oil well driller, with an irrelevant past medical history, has had typical attacks of paroxysmal tachycardia since he was 20 years of age. Until the last three years the attacks were mild and infrequent, occurring about once a year and lasting from a few minutes to two or three hours. During the last three years the attacks have occurred on an average of once in two months and last from fifteen to thirty hours. During the last three attacks, alarming symptoms of acute circulatory failure, i. e., marked venous congestion, orthopnea, marked cardiac distress, cyanosis, and a feeble uncountable pulse with a heart rate around 250 a minute, have developed near the end of the attacks. He complains of agonizing precordial pain, when the attack suddenly ceases. Between the attacks the patient has no symptoms referable to the cardiovascular system, no evidences of cardiac disease are demonstrable by ordinary clinical means, and the patient enjoys robust health. In the recent attacks none of the ordinary means of vagus stimulation have had any influence on the condition. Choline chloride was tried once without any effect. Can you suggest any treatment that might be useful in terminating these attacks. Would continuous administration of quinidine be indicated in hope of preventing the condition. Kindly omit name.

M.D., Wyoming.

ANSWER.—A heart that can stand the stress of the rapid rate of an auricular paroxysmal tachycardia at the age of 20 cannot do so as readily at 51. At that age there are usually changes of some degree in the coronary arteries and in the heart muscle and the conducting tissues, which make such a rapid rate a more serious matter. A rate of 250, however, is too rapid a rate to maintain an adequate circulation at any time, and attacks lasting from fifteen to thirty hours, even with a slower rate, usually show evidence of circulatory failure.

If it is possible to obtain an electrocardiogram during an attack, it would be interesting to see what it would show. The same case that showed a typical tracing in early life may show aberrant ventricular complexes during the attack in later years, with bundle branch block or even a condition resembling a ventricular tachycardia. Attacks of auricular fibrillation may be interspersed with attacks of paroxysmal tachycardia. A rate of 250 is much more rapid than is found in auricular paroxysmal tachycardia, which rarely goes over 200. An auricular flutter, with 1:1 block, should be ruled out. Quinidine in daily doses, adequate to prevent the attacks, is indicated. It should be discontinued at once, however, if there are any evidences of untoward results. Morphine may be of use during the attacks or vagus (carotid sinus) stimulation may be more effective after the morphine.

At the end of an attack there is often a slow, irregular pulse with long pauses between the beats, and anginal pain may occur consequent on the decreased coronary flow.

CYST OR GANGLION OF GREAT TOE

To the Editor:—A man about 40 years of age came to me about two months ago with a tender swelling on the inside of the left great toe about one-fourth inch from the nail. Thinking it was an abscess I incised it, and to my surprise several drops of a jelly-like fluid came out. It was light colored and a good deal like the vitreous of the eye. A few days ago he came in again and said that since the previous visit the swelling had recurred several times, and each time he had opened it up and the same kind of fluid escaped. I was unable to probe it to any depth, so incised the tumor and curetted the wound. Now after a lapse of ten days it still continues to drain and does not heal. I can find nothing in my books to give me an indication of what it is and have asked other physicians but they say they do not know. Can you tell me what it is and the proper treatment. I would appreciate your help greatly.

A. W. PATTERSON, M.D., Fonda, Iowa.

ANSWER.—This condition is doubtless a cyst, which is exactly similar to that which frequently develops over the dorsal aspect of the wrist and is commonly known as a ganglion.

Concerning the origin of these cysts there is considerable dispute. By some they are considered extrusions of the synovial membrane of a joint or of the synovial lining of a tendon sheath. By others they are considered a degenerative process arising in the fibrous tissue of the joint capsule or fibrous tissue overlying a bone. The cysts that form alongside the nail of the fingers or toes can often be traced by careful dissection to the region of the distal interphalangeal joint and may arise from this joint.

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The proper treatment is careful excision of the entire cyst wall. This excision can be accomplished with the help of an adequate skin incision and of a bloodless field, secured with the help of a blood pressure band or a tourniquet. Unless one can visualize the involved area exactly, it is easy to leave a small portion of the cyst wall behind and have a recurrence of the trouble.

FACIAL FLUSH IN TUBERCULOSIS

To the Editor:—Many years ago, while on duty in a government hospital for the tuberculous, I was impressed with the observation that, when a tuberculous patient flushes, the color in his face appears in streaks or splotches alternating with streaks or splotches of a pallid hue. This streaking of the face has no relation, in appearance at least, to the familiar hectic flush, nor is it the pallid condition about the lips and nostrils observable in almost any very ill patient. These last named conditions have often been described, as has the peculiar facial expression of the tuberculous. Standard textbooks devote pages to this subject, yet the condition of which I speak has never, so far as I have been able to learn, been mentioned in literature. When a person in health flushes, as from exertion, coughing or blushing, the increased color in his face is uniform. When such a person turns pale, as from shock, fright or in a faint, the blanching is uniform. Not so with the tuberculous. I have observed this coloring in streaks chiefly in ambulatory patients and have observed it with sufficient frequency to be convinced that it is always present in patients with advanced pulmonary tuberculosis. I am convinced that the condition is an indication of pulmonary disease, but I do not know that it is more marked in tuberculosis than in pulmonary impairment due to other causes. To what extent the condition is the result of a vasomotor disturbance, or to what extent it is due to defective aeration, I have not been able to determine. The condition may be observed by simply having the patient lower his head for a few moments, or by having him cough. He should be under a good light. I am asking that clinicians who see a large number of pulmonary cases look out for and report on this sign, which may or may not prove to be of value in diagnosis.

BENJAMIN K. HAYS, Oxford, N. C.

ANSWER.—Formerly, it was believed that the hectic flush is due to toxemia. However, it was observed that the flush is often unilateral and always on the side of the diseased lung. When both lungs are diseased, the flush is more marked on the side of the greater activity of the disease. If the condition were due to toxemia, one would expect both sides of the face to be flushed to an equal degree. Therefore this phenomenon has been explained on a reflex basis. When the sensory fibers of the trigeminus nerve are stimulated, dilatation of the vessels occurs in the area which these fibers supply. The irritation produced by disease in the lung results in stimuli which pass over the afferent fibers of the vagus nerve. In the trigeminus nerve there are dilator fibers of cerebral origin. Thus, the impulses carried over the vagus from the area of disease pass reflexly over the trigeminus nerve, to result in dilatation of the blood vessels, giving the hectic flush. Such a flush or burning sensation over other parts of the body, such as the lobe of the ear or even the skin over the chest wall, may be brought about in the same manner but over different nerve paths. Just why the color in a tuberculous patient's face appears in streaks or splotches alternating with streaks or splotches of a pallid hue is difficult to explain. In such a case there probably is some defect in the vasomotor mechanism, possibly due to afferent impulses from the irritated lung, since other reflex disturbances, such as those mentioned, spasticity of muscles, and so on, are also observed. Defective aeration probably could have such an effect only by affecting the vasomotor mechanism. As was mentioned, further observation of a large number of cases will be necessary to determine whether the impairment is always due to tuberculosis or other pulmonary diseases.

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BLACK TONGUE AND HALITOSIS

To the Editor:—For more than twenty years a patient has had on the posterior part of the tongue a grayish thick covering with a strong foul smell. The patient is now about 40 years old. The reaction of the saliva is slightly acid. With an alkaline mouth wash the patient gets a stomatitis. Weak solutions of boric acid and Burow's solution burn; chamomile flower tea, a teaspoonful to a glass of water, is well tolerated. Internal iodide medication had to be dropped repeatedly, as signs of intolerance developed. Brushing the tongue morning and night with a soft toothbrush has been tried with no success as yet. Aside from the described condition the patient has a vasomotor rhinitis. May I ask you for advice as regards the treatment and is there any hope for cure of this condition? Kindly omit name and address.

M.D., New Jersey.

ANSWER.—Bad odor of the breath associated with either coating of the tongue or a hypertrophy of the papillae just in front of the circumvallate papillae and in the median line is not a rare condition. Apparently the odor is generated by a growth of fungi about the base of the elongated papillae or beneath the coating. The condition described may be a variety of the clinical entity known as black tongue, as the pigmentation in this defect varies from brownish black to light gray. Foul odors emanating from the mouth as well as from the nose occur in such forms of atrophic rhinitis as ozena but not in vasomotor rhinitis. In any event, treatment is indicated only for the purpose of eliminating the bad odor. Usually thorough swabbing of the region with strong hydrogen dioxide followed by irrigation with warm physiologic solution of sodium chloride is effective if repeated a number of times. In stubborn cases a suitable brush with soft bristles may be used, but, because the foul smelling deposits are located at the base of the papillae, patience and persistence are required. In obstinate cases of black tongue, Prinz (Diseases of the Mouth and Their Treatment, Philadelphia, Lea & Febiger, 1935, p. 436) recommends the use of a 10 to 15 per cent solution of salicylic acid in equal parts of alcohol and glycerin, applied on a swab and followed by irrigation with salt solution. The use of scrapers or other methods of mechanical removal has been advocated, but, as Prinz warns, such treatment is likely to promote recurrence.

URTICARIA DURING MENSTRUATION

To the Editor:—A married woman, aged 30, gives a negative history as to illness, other than having had an operation for anchoring the uterus about two years ago. She has been married for five years and has had three abortions, one being followed with a tubal infection, which required a month's treatment to clear it up. A few months later she noticed that around her menstrual period there were several fair sized swellings, below the knees, to the ankles. These swellings are painful when they develop and are at first red and after about three days become bluish. After the operation she did not notice them for several months but she has had them again for the past several periods; now they develop all along the inner side of the left thigh, although formerly both legs were affected. The bluish discoloration did not entirely disappear the last time and there is still some tenderness where the swellings were and an area about the size of a half dollar at each site. Her last period was about two weeks ago and she expects the same condition at the next period. There is no swelling of the feet or ankles and when a tourniquet is used at the top of the thigh the areas do not swell as a varicosed vein does, although she states that in the morning when she is first out of bed the swellings are smaller and increase in size during the day. One physician told her that they were due to allergy and dieted her without results and another one told her they were due to the condition of her uterus and that after an operation she would be cured. She was relieved for a few months but has had this condition again for several months. I cannot find any mass in the pelvis but there is some tenderness about the left side of the uterus, which is larger than normal and down lower in the pelvis than normal. I expect to see her again when these swellings develop and wish you would give me your opinion as to what is the cause of this trouble. It seems that they may be due to an old phlebitis, which developed a month or two after a salpingitis, but I cannot make the veins distend so that I can be certain about it, and the location of the swellings is not exactly along the course of the veins, as they are scattered about the surface of the thigh. The patient states that when they are swollen they are rather hard and they will pit on pressure. The urine is normal. Kindly omit name and address.

M.D., Minnesota.

ANSWER.—The lesions described sound like either erythema multiforme or giant urticaria.

If, as suggested, there is a definite relationship between menstruation and the appearance of the nodules, erythema multiforme is unlikely.

Recurrent attacks of urticaria sometimes accompany menstruation, notably in patients with pelvic disorders. In the majority of such cases, disturbances of the alimentary tract are present also and the recurrence of the nodular swellings may be prevented by careful attention to diet and to elimination.

EXERCISE TOLERANCE TESTS

To the Editor:—Please state the significance of the exercise tolerance test from an insurance standpoint in regard to the pulse rate and blood pressure not increasing after exercise or increasing to an excessive degree.

M.D., South Carolina.

ANSWER.—Life insurance companies, although they have been greatly interested in the development of tests of circulatory efficiency that are significant from the standpoint of prognosis, have been unable as yet to arrive at any test or group of tests of definite value in this field. In fact, many medical directors are becoming dubious about ever being able to do so.

In general the pulse rate and the blood pressure are expected to increase after exercise. Failure of the blood pressure to do so may indicate a poor cardiovascular reaction or a very stable vasomotor system, while little or no increase in the pulse rate is considered a favorable reaction. It is assumed also that the pulse rate should return to the preexercise rate within two minutes after the prescribed exercise. If it does not do so, further study of the circulatory condition is indicated; but the finding in itself warrants no definite unfavorable conclusion.

In other words, the reaction to exercise is just one of the many points to be considered in arriving at an estimation of the condition of the cardiovascular system.

PERSISTENT FURUNCULOSIS

To the Editor:—A man, aged 51, has suffered from multiple furunculosis, involving any portion of the body, for eighteen years. He is a foreman in a paper and rag warehouse but does little or no hard work himself. While it may seem at first that the dusty atmosphere may be an etiologic factor in his condition, may I remark that he has had boils even when away to the country and when at home away from work for a period of a month. He has been treated with regard to hygienic measures, such as daily bathing with bland soaps and daily change of underclothing, and attention to bowel regulation. He has had all the vitamins in high dosage; also calcium compounds in high dosage, liver and iron. He uses a sun ray lamp at home, which I ordered and have graduated the dosage slowly and progressively for full body exposures. He has had numerous parenteral treatments with vaccines both stock and autogenous, nonspecific therapy, staphylococcus toxoid, and bacteriophage made from culturing his own pus from the furuncules. (The organism, incidentally, has always been Staphylococcus aureus.) He has had large doses of tin oxide tablets and sulphur by mouth. Diet has likewise been to no avail. The boils have varied greatly in size; the largest are about 9 cm. in diameter. The patient weighs 201 pounds (91 Kg.) and is 5 feet 9 inches (175 cm.) tall. Physical examination is negative. The blood count is normal, as is the blood chemistry, including sugar, urea and creatinine. Frequent urinalysis is negative. He takes no medication such as might cause or favor skin eruptions. The blood Wassermann reaction is negative. I know of nothing further that I can do for this man. Have you any suggestion as to etiology and therapy? Please omit name.

M.D., New York.

ANSWER.—Persistent furunculosis lasting over eighteen years is rather unusual. After a series of furuncles there is usually a rise in the body immunity, which effectively overcomes the infection and protects the individual.

In this instance an effort must be made to raise the skin resistance, as metastatic infection in other tissues has not developed.

It seems that most of the well known remedies and some very doubtful remedies as well have been tried except the use of the x-rays. Several authors report the beneficial effects of roentgen treatment. It has proved helpful in aborting furuncles, in hastening their healing and in stimulating resistance to protect against infection.

It should be used in conjunction with surgery in the larger furuncles but may prove more valuable here as a preventive of further infection. The exposure should be made under the supervision of a competent roentgenologist.

The intracutaneous method of administration of vaccine or toxoid is believed to be superior to the subcutaneous route, through stimulating the immunizing bodies in some specific manner. This should be tried at least in resistant cases.

The actual details of personal hygiene should be outlined and checked up repeatedly. Since furunculosis is the result of skin infection, some method of staphylococcus destruction by antiseptics should have some value here, in addition to cleanliness and avoidance of irritation or friction by clothing.

It may be of value to apply an ointment to the skin with or without an antiseptic after bathing.

Regardless of the normal blood sugar, the carbohydrates and sugars should be reduced to a minimum.

PROSTATITIS AND ASSOCIATED SYMPTOMS

To the Editor:—A white man, aged 40, had a prostatic abscess of idiopathic origin five years ago, which ruptured spontaneously and drained through the urethra. He had vague discomfort in the perineum following this, which at times became a heavy ache, which radiated into the right leg. He had only a few massages of the prostate at the time. During the past year and a half the patient has had migraine-like attacks with typical aura, scintillating photophobia, increase of nervousness, dull boring headache, sometimes bilateral, and finally nausea. These attacks have varied greatly in frequency and severity. When more frequent they are less severe. The worst ones ended by vomiting. About one year ago he had two very light prostatic massages on different days, each of which was followed by atypical attacks of migraine within two hours. The prostatic secretion was essentially normal under the microscope. Since then no massages have been given. The attacks continue and at times incapacitate the patient for twenty-four hours. Is it probable that these attacks are caused by the prostatitis? What method of treatment would you advise in such a case? Are vaccines valuable? Is there any form of heat to the gland worth while? Kindly omit name.

M.D., Indiana.

ANSWER.—In rare instances nervousness, headaches and dizziness may be due to chronic infections in the prostate gland, so that this symptom complex may be due to a chronic prostatitis, although this is exceedingly rare. On the other hand, the fact that the patient does not have pus in the prostatic strippings when examined with the microscope would lead one to believe that the prostate is normal and hence not a factor. On the other hand, the fact that light prostatic massage produces these atypical attacks of migraine must necessarily cause one to stop, look and listen. Because of this occurrence, further investigation of the prostate is indicated; that is, the prostate should be massaged at weekly intervals and the strippings examined with the microscope. If the strippings show no pus, obviously there is no infection of the prostate that can be drawn into the picture. Without this, the natural impression would be that the attacks of migraine following massage are purely accidental. If there is no pus in the prostate, no treatment would seem to be called for. If, however, repeated examinations of the strippings show pus, heat by rectum and massage should be employed. Whether or not vaccines are indicated will depend entirely on whether cultures from the strippings show infection.

SPONTANEOUS IDIOPATHIC PNEUMOTHORAX

To the Editor:—A man, aged 30, worked at the clinical thermometer trade for some eleven years. During this time he did much glass blowing in molding the bulbs for thermometers. Before starting his day's work on this particular date he was suddenly seized with a severe pain, referred to the abdomen. The diagnosis was finally collapse of the right lung. The day before the lung collapse he stated that he was blowing through much finer tubes than usual and that extra effort was required. However, he does not recall any particular time when he felt any sensation other than that due to slightly increased effort. Was the lung collapse caused directly or indirectly by his occupation? Was the collapse aggravated by his occupation? His previous health was excellent. Please omit name.

M.D., New York.

ANSWER.—Pulmonary emphysema is a frequent occupational disease lesion in work people who are required to practice deep and forceful inspiration and expiration. In glass blowers and players of wind instruments, among other trades people, through slow changes in the lung tissues, the lungs lose their normal elasticity and the alveoli become distended so that the occurrence of a spontaneous pneumothorax is favored.

The etiology of spontaneous idiopathic pneumothorax is still uncertain. It may occur without any immediate obvious cause or may arise in the course of more or less violent effort in a patient up to then apparently well. About 16 per cent of all cases arise as a sequel to well characterized emphysema. In the absence of known diseases it is quite reasonable to suspect glass blowing to have been a factor in the causation of this spontaneous pneumothorax. A number of actual cases are on record, appearing, however, for the most part in foreign publications:

Krankheitforschung **9:** 1 (Jan.) 1931.
Zentralbl. f. Gewerbehyg. **11:** 7 (Jan.) 1934.
Gig. bezopass. i pat. truda. **8:** 60, 1930.
Nederl. tijdschr. v. geneesk. **76:** 2905 (June 11) 1932.
Vrach. delo. **14:** 1091 (March), 272 (Oct.) 1931.

Additional information may be found in:

J. Clin. Investigation **13:** 295 (March) 1934.
Am. J. M. Sc. **183:** 695 (May) 1932.

SIMULTANEOUS DIPHTHERIA AND SCARLET FEVER

To the Editor:—I should like very much to know what the possibilities are of diphtheria and scarlet fever occurring in one patient at the same time. Have these two diseases occurred in one person, and what is the relative frequency? Please omit name. M.D., Iowa.

ANSWER.—Diphtheria and scarlet fever may occur in the same patient at the same time. It is not uncommon that both diseases are present in patients admitted to hospitals for acute infectious diseases. Of 1,039 patients with scarlet fever admitted to the Edinburgh City Hospital twenty, or nearly 2 per cent, had concurrent diphtheria (Ker: Infectious Diseases, 1909). Of 14,025 patients with acute infectious diseases, mostly children, admitted to the Durand Hospital from 1913 to 1933, eighty had scarlet fever and diphtheria on admission (Weaver, G. H.: Medical Report of the Durand Hospital of the John McCormick Institute for Infectious Diseases for Twenty Years 1913-1933). In this group of cases it would be difficult and in many cases impossible to decide whether the infections developed at the same time or one after the other. Diphtheria may develop as a secondary infection in scarlet fever and vice versa.

TEMPERATURE OF FLUID FOR PHLEBOCLYSIS

To the Editor:—I am about to write a paper on the problem of maintaining a uniform temperature in infusions. I would appreciate any information you can send me concerning medical opinion as to the proper temperature, the method of regulating, and the results with the method now in use.

SISTER M. CARMELITA, R.N., Convent Station, N. J.

ANSWER.—With the modern drop by drop method of phleboclysis, the matter of temperature of the fluid to be injected is generally considered relatively unimportant. It is certainly much less important than is slowness of infusion. It is never-

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theless of possible advantage to introduce hot fluid, even up to the point of 110 F., if the patient's temperature is subnormal. To maintain such temperature safely at the point of delivery, Paul Titus (A Combined Needle Adapter and Thermometer for Intravenous Infusions, THE JOURNAL, May 19, 1934, p. 1676) has devised a needle adapter and thermometer. In general the practice of maintaining the temperature in the container at 120 F. ensures delivery into the vein at a temperature of not less than 100 F. If the patient has a high temperature, the solution in the container may be at room temperature.

DERMATITIS FROM ENAMELS

To the Editor:—I should like to know whether you have any information regarding what chemicals are present in Cook's Baking Enamel that would produce a very severe dermatitis. I have a patient who has worked in the enameling department of a large corporation for the last eleven years without any trouble. The firm changed the kind of enamel it was using and in three or four days the patient had a severe dermatitis of the arms and feet. Any information you can give me regarding this will be appreciated. HENRY F. HYNDMAN, M.D., Wichita, Kan.

ANSWER.—The number of possible combinations of the many constituents in Cook's baking enamels aggregates a thousand. This does not mean that a thousand dissimilar chemicals enter these products but instead that the twenty-five or more constituents through quantitative variation may lead to a thousand different formulas. Among other constituents are toluene, xylene, petroleum distillates, (rarely) turpentine, glycerin, phthalic anhydride, butyl acetate and butyl alcohol. Almost any of these ingredients might lead to a dermatitis, particularly in persons with increased susceptibility to the action of chemical irritants. It is not possible to advise in this instance that a change be made to any particular type of enamels, since all contain similar ingredients and all are likely to lead to at least an occasional case of dermatitis.

INDICATIONS FOR CESAREAN OPERATION

To the Editor:—A primipara, aged 28, has the following external pelvic measurements: interspinous, 20 cm.; intercristal, 27 cm.; conjugate, 17 cm. She does not show anything else abnormal. I have not as yet made a definite attempt to make internal measurements. Would you try to let this woman deliver at term or would you do a cesarean operation? Please omit name. M.D., Texas.

ANSWER.—The external measurements have but little value in determining the size of the pelvis, although a diagonal conjugate of 17 cm. would indicate some contraction in the anteroposterior diameter; but one is not justified in performing a cesarean section on external measurements alone, even if they are small. Nature will terminate 75 per cent of cases of contracted pelvis unaided or helped by a simple low forceps operation.

This patient should have a careful, competent internal pelvic mensuration and, unless a high degree of pelvic contraction is discovered, she should be given a good conscientious test of labor. Entirely too many cesarean sections are being done on the basis of the slimmest indications.

POISONING FROM OLEANDER AND YUCCA PLANTS

To the Editor:—Will you kindly inform me whether the oleander or yucca plants of Florida can cause a dermatitis which is similar to that produced by ivy poisoning in the North?

EDWARD J. KEMPF, M.D., Eustis, Fla.

ANSWER.—No reports have been found of a dermatitis simulating "ivy poisoning in the North," produced by the oleander or yucca plants of Florida. The yucca plant is apparently nontoxic. The oleander shrub has been reported as producing poisoning in children and adults. In the case of the oleander, a milky juice exudes from the leaves when punctured, and this juice has poisonous properties.

TYPHOID VACCINATION AND ENCEPHALITIS

To the Editor:—Please give me an opinion as to the advisability of revaccination with vaccinia and triple typhoid of a patient with epidemic (lethargic) encephalitis of the Parkinson type, ten years arrested, in good general condition except for frequent "ocular spasms." He is planning a sea voyage through the Canal Zone and way points.

DELL T. LUNDQUIST, M.D., Palo Alto, Calif.

ANSWER.—There is no apparent good reason why the patient should not receive the vaccines mentioned.

Medical Examinations and Licensure

COMING EXAMINATIONS

AMERICAN BOARD OF OPHTHALMOLOGY: The Cincinnati examination previously announced will not be held. The next examination will be given in St. Louis, Nov. 18. *Application must be filed before Sept. 15.* Sec., Dr. William H. Wilder, 122 S. Michigan Ave., Chicago.

American Board of Otolaryngology: Cincinnati, Sept. 14. Sec., Dr. W. P. Wherry, 1500 Medical Arts Bldg., Omaha.

AMERICAN BOARD OF PEDIATRICS: Seattle, Aug. 8, Philadelphia, Oct. 10, and St. Louis, Nov. 10. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF RADIOLOGY: Detroit, Dec. 1-2. Sec., Dr. Byrl R. Kirklin, Mayo Clinic, Rochester, Minn.

NATIONAL BOARD OF MEDICAL EXAMINERS: The examination will be held in all centers where there are Class A medical schools and five or more candidates desiring to take the examination, Sept. 16-18. Ex. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

NEVADA: Reno, Aug. 5. Sec., Dr. Edward E. Hamer, Carson City.

NEW HAMPSHIRE: Concord, Sept. 12-13. Sec., Board of Registration in Medicine, Dr. Charles Duncan, State House, Concord.

NEW YORK: Albany, Buffalo, New York and Syracuse, Sept. 16-19. Chief, Professional Examinations Bureau, Mr. Herbert J. Hamilton, 315 Education Bldg., Albany.

OKLAHOMA: Oklahoma City, Sept. 10-11. Sec., Dr. James D. Osborn Jr., Frederick.

PUERTO RICO: San Juan, Sept. 3. Sec., Dr. O. Costa Mandry, Box 536, San Juan.

Connecticut March Examination

Dr. Thomas P. Murdock, secretary, Connecticut Medical Examining Board, reports the written examination held in Hartford, March 12-13, 1935. The examination covered 9 subjects and included 70 questions. An average of 75 per cent was required to pass. Twenty-one candidates were examined, 17 of whom passed and 4 failed. Eleven physicians were licensed by endorsement. The following schools were represented:

PASSED School	Year Grad.	Per Cent
Yale University School of Medicine	(1929)	84.9
Georgetown University School of Medicine	(1932) (1934)	75, 78.2* 80.2*
Boston University School of Medicine	(1933)	77.2, (1934) 78.1*
Tufts College Medical School	(1934)	82.1,* 86.3*
Washington University School of Medicine	(1933)	82.1
Columbia University College of Physicians and Surgeons	(1934)	80.8, 84*
Cornell University Medical College	(1932)	83.9
Long Island College of Medicine	(1934)	82.9
University of Wisconsin Medical School	(1934)	79.7
Queen's University Faculty of Medicine	(1934)	81.1*
Magyar Királyi Pázmány Petrus Tudományegyetem Orvosi Fakultasa, Budapest	(1931)	75†
Regia Università di Napoli Facoltà di Medicina e Chirurgia	(1933)	78.3

FAILED School	Year Grad.	Number Failed
George Washington University School of Medicine	(1934)	1
University of Texas School of Medicine	(1933)	1
Osteopaths‡		2

LICENSED BY ENDORSEMENT School	Year Grad.	Endorsement of
Rush Medical College	(1934)	N. B. M. Ex.
Tufts College Medical School	(1930) (1932)	New Jersey, Vermont
University of Michigan Medical School	(1931)	Michigan
Columbia Univ. College of Physicians and Surgeons	(1929)	New York
Cornell University Medical College	(1933)	N. B. M. Ex.
Duke University School of Medicine	(1933)	N. B. M. Ex.
Vanderbilt University School of Medicine	(1931)	Tennessee
University of Virginia Department of Medicine	(1926)	New York
Marquette University School of Medicine	(1934)	N. B. M. Ex.
University of Wisconsin Medical School	(1927)	Michigan

* License has not been issued.
† Verification of graduation in process.
‡ Examined in medicine and surgery.

Hawaii April Examination

Dr. James A. Morgan, secretary, Board of Medical Examiners, reports the written examination held in Honolulu, April 8-11, 1935. The examination covered 10 subjects and included 55 questions. An average of 75 per cent was required to pass. Three candidates were examined, one of whom passed and 2 failed. The following schools were represented:

PASSED School	Year Grad.	Per Cent
University of Pennsylvania School of Medicine	(1932)	83

FAILED School	Year Grad.	Per Cent
Chicago Medical School	(1920)	75*
Loyola University School of Medicine	(1934)	74

* Failed in three subjects.

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Book Notices

A Manual of Obstetrical and Gynaecological Pathology. By John H. Teacher, M.D. Edited by Alice J. Marshall, M.B. Cloth. Price, $15.25. Pp. 407, with 320 illustrations. New York & London: Oxford University Press, 1935.

This contribution to the specialty of obstetrics and gynecology was planned and outlined by Professor Teacher prior to his death. He had also prepared nine chapters for the work, which chapters have been edited carefully by Alice J. Marshall, who had been previously a co-worker with Professor Teacher. The author acknowledges a considerable debt to Professor Frankl, whose work on gynecologic pathology influenced him considerably. The editor has carefully scrutinized and revised the original chapters of Professor Teacher and accumulated new material from relevant notes and papers that were placed at her disposal by Mrs. Teacher. The illustrations have been carefully selected, and most of them represent microscopic changes. A considerable portion of the volume is devoted to a consideration of histology and embryology in relation to cyclic changes and other physiologic alterations associated with menstruation, ovulation and early and late gestation. Aside from the pathology of the placenta and the membranes, little attention is given to pathologic changes relative to the fetus. Various other authorities have contributed to this careful work. A consideration of the bacteriology of the genital tract has been presented by Robert Cruickshank. The author has included a short chapter on technic. This pertains particularly to the collection and primary preservation of tissues and should be of help as a guide to the surgeon in securing and transmitting tissues in their proper manner to the laboratory for microscopic examination. Teacher was so well qualified on account of his studies that the chapters pertaining to cyclic changes, pathology of the endometrium and the implantation and early development of the ovum, together with consideration of early abortions, are in themselves almost classic. One cannot give detailed consideration to the various other chapters in the book but, on the whole, one has a feeling that less attention is given to a consideration of the gross pathology than to the microscopic. The volume would therefore be of much greater value to those who are interested in the microscopic appearance of genital lesions. It constitutes an excellent work on the histopathology of the female generative tract and is well worthy of careful scrutiny. It would, of course, be impossible to include within the pages of the volume all the gross and microscopic pathology of the female generative tract. The authors have concentrated and succeeded in making a definite contribution to current literature.

Traité de gastroscopie et de pathologie endoscopique de l'estomac. Par François Moutier, chef de laboratoire de la Faculté de médecine. Préface du Professeur P. Duval. Travail de la clinique de thérapeutique chirurgicale de la Faculté de Paris (Professeur: Pierre Duval). Paper. Price, 120 francs. Pp. 347, with 113 illustrations. Paris: Masson & Cie, 1935.

This excellent work constitutes the first atlas of gastroscopy since Schindler's atlas appeared in 1923. Duval has written the preface, in which he calls special attention to the fact that gastroscopy has now become an indispensable clinical method. Moutier, whose many papers on gastroscopic problems are well known, follows closely in the technical part the statements of the German authors and gives a precise description of the modern flexible gastroscope and its use. He underlines the sentence that danger in gastroscopy is only of historical importance in that it existed for the rigid instruments but not with the modern flexible gastroscope. An exact description of the normal gastric mucous membrane is given. It is important to note that Moutier does not hesitate to enumerate the various possibilities for being mistaken and for considering as pathologic formations that are quite normal. In a method such as gastroscopy, in which the subjective factor is large, such mistakes are always possible and must be avoided. These chapters on the normal gastric membrane show the great advance in our knowledge of the gross anatomy of the stomach resulting from the use of the gastroscope. In the sections dealing with pathologic alterations, Moutier describes carefully and critically the great variety of pictures that are well known to every gastroscopist. In an important chapter on chronic gastritis Moutier goes his own way, subdividing this disease on a purely anatomic basis. The chapter on syphilis is of special value, because no similar observations exist in the gastroscopic literature. The sections on the benign gastric ulcer and tumors are lengthy and well written. In the chapter on the postoperative stomach Moutier confirms the observations of earlier authors, all of whom noted the frequency of an extremely severe chronic gastritis. He shows such pictures as well as several jejunal ulcers. This book will doubtless have a profound influence in aiding the introduction of gastroscopy as a safe routine clinical method and in affecting the conceptions of gastric disease in French speaking countries, as the German gastroscopists did in German speaking countries many years ago.

Aids to Embryology. By Richard H. Hunter, M.D., M.Ch., Ph.D., Lecturer in Anatomy, Queen's University, Belfast. Second edition. Cloth. Price, $1.25. Pp. 172, with 39 illustrations. Baltimore: William Wood & Company, 1934.

The chief object of this little book and others in the same series is to provide a summary of the facts needed by medical students in order to pass the examinations set in Great Britain. It should be useful to others who wish to review the subject for similar purposes. There have been some additions and considerable revision of the first edition. The subject is presented only so far as it helps in the understanding of adult relations and of abnormalities in development. The chief problems of general embryology are outlined (twinning is omitted, however) and the development of the fetal membranes and of the various systems of organs in man are described. Considering the small amount of space available, the author has succeeded admirably with the help of a series of clear simple diagrams. Under the circumstances, ambiguities are unavoidable. Thus the definitions of the chorion frondosum and anencephaly give false impressions. Attention should be called to certain faults. The accounts of the menstrual cycle and of the central nervous system are not abreast of present knowledge. All "blue babies" are explained on the basis of the patency of the ductus arteriosus. The statement that true hermaphroditism has not been found in man is incorrect.

Handbuch der Kinderheilkunde: Ein Buch für den praktischen Arzt. Herausgegeben von Geh. Med.-Rat Prof. Dr. med. M. v. Pfaundler, Direktor der Kinderklinik in München, und Geh. Med.-Rat Prof. Dr. med. A. Schlossmann, Direktor der Kinderklinik im Düsseldorf. Band X: Die Hautkrankheiten des Kindesalters. Bearbeitet von J. Becker et al. Fourth edition. Paper. Price, 169 marks. Pp. 884, with 383 illustrations. Berlin: F. C. W. Vogel, 1935.

This work needs no introduction to the medical world. The tenth volume has all the merit of the preceding volumes and not only complements them but also forms an important independent addition to the literature of pediatrics and dermatology. The first edition of the Handbuch, which appeared almost thirty years ago, contained a restricted section on skin diseases of childhood. In the preparation of the second edition, four years later, it became apparent that a special volume on skin disorders was necessary, and this was to have been edited by Schlossmann. The World War, the death of Leiner who was to have been the main contributor, the illness of Schlossmann, and other circumstances delayed the appearance of the special volume. After Schlossmann's death in 1932 the preliminary work was taken up again and carried forward under great difficulties. Dermatologists experienced with the dermatoses of children, and pediatricians interested in skin diseases have contributed to the volume. It is thus a product of expert contemporary thought in both pediatrics and dermatology. In accordance with the basic principles on which the "Handbuch" was constructed, the main emphasis is on practical diagnostic and therapeutic questions. The authors consider those dermatoses which occur only in childhood and also those which have special symptoms and characteristics in this period of life, though occurring at all ages. No attempt is made to maintain a strict systematic classification, because this presents many difficulties. In a book of this kind some overlapping in the various articles is unavoidable, but the editors have taken precautions to reduce reduplications and contradictions as far as possible. That certain authors touch on subjects which are

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considered more fully by another (Pringle's disease, Schüller-Christian syndrome) is due to differences of opinion as to the origin and nature of these conditions. Attention is called to erythema annulare rheumaticum (Lehndorff-Leiner), page 584, which receives fuller treatment than has heretofore been accorded it. This book is in the same format as the other volumes and is richly illustrated. Attention should be called to the many excellent colored plates, which are of special value in the study of skin diseases. The full table of contents, nine pages long, the marginal outline notes, the clear divisions and subdivisions of the material, and the many bibliographic citations at the end of each chapter make this a handy book to use. As the work is chiefly valuable for reference, a good index is desirable, and the subject index, compiled by Dr. Erna Eckstein-Schlossmann, appears to be entirely adequate. However, many will feel keenly the lack of an index of proper names. The book is a noteworthy contribution to the study of skin diseases in childhood. It is one of the most important contributions of the year to the pediatric literature.

The Curriculum in Sports (Physical Education). By Seward C. Staley, Professor of Physical Education, University of Illinois. Cloth. Price, $2.50. Pp. 373. Philadelphia and London: W. B. Saunders Company, 1935.

This is designed primarily as a textbook for students and teachers of physical education or, as the author prefers to call it, sports education. A considerable portion of the first half of the book is devoted to a philosophical discussion of education and physical education in general, to a review of the history of physical education, and to a defense of the substitution of the term sports education for the conventional physical education. The author argues that physical education in the literal sense is impossible and that consequently the use of the term is unjustified. Gigantic sports events and competitions primarily for the entertainment of the public are condemned as an abuse of the function of the school. In enumerating the objectives of the physical activities program, the author emphasizes mental and social values as well as physical development. The most useful portion of the book is a detailed consideration of the formulation of a curriculum of sports education with suggestions concerning activities, instructional methods, and procedures for measuring accomplishment. As this is distinctly a textbook and not easy reading, it probably will have little interest for the general reader; but it should be distinctly useful to those engaged in this aspect of education.

Sammlung psychiatrischer und neurologischer Einzeldarstellungen. Herausgegeben von Prof. Dr. A. Bostroem und Prof. Dr. J. Lange. Band V: Konstitution und Prozess in der Schizophrenie. Von Medizinalrat Dr. Skalweit, Privatdozent für Psychiatrie und Neurologie an der Universität Rostock. Paper. Price, 4.50 marks. Pp., 88, with 6 illustrations. Leipzig: Georg Thieme, 1934.

This volume is a complete analysis of the process of schizophrenia as analyzed by means of the Rorschach test, the observations being correlated at the same time with the body structure types of Kretschmer. The study consists of an analysis of ninety chronic cases and twenty-three acute cases. The chronic cases are tabulated individually; the acute cases are also studied by themselves, and the type of intelligence and the "life type" of each is analyzed. The third part of the research consists in a direct investigation by means of the Rorschach psychogram of the patient's status in different periods of the disorder. In this part the data are tabulated and case histories are presented. Section III is especially interesting, for it shows certain factors that have not been indicated by previous investigators as regards the form of the psychosis. The speed of its course and other features of the mental disorder have only been suggested by previous studies but are here gone into more deeply. The report concludes with a ten point summary in which the author attempts to show various differences between the schizoid make up and the manic-depressive make up, as well as the nature of the basic defect of the schizophrenic. The work is a contribution to our knowledge of this disorder but is of more value to psychiatric research workers than to psychiatric clinicians, for the style is complicated and a knowledge of the basic technics of Rorschach and of the postulates of Kretschmer is presumed.

Veterinary Helminthology and Entomology: The Diseases of Domesticated Animals Caused by Helminth and Arthropod Parasites. By H. O. Mönnig, B.A., Dr.Phil., B.V.Sc., Professor of Parasitology, Faculty of Veterinary Science, University of Pretoria. Cloth. Price, $9. Pp. 402, with 264 illustrations. Baltimore: William Wood & Company, 1934.

This was written especially as a textbook for veterinary students, but it lists fifty-seven parasites affecting man. Forms that are relatively unimportant from the veterinary aspect, such as Necator americanus, are accorded but little space. Parasites of veterinary significance are discussed briefly as to life cycles, pathogenicity, symptoms, diagnosis, treatment and prophylaxis. A convenient host-parasite list gives all the parasites of each host, together with the page reference. The book is not intended to be a complete and exhaustive treatise on all human and animal parasites. As a ready reference work for the more important forms, it should be of service.

Les encéphalites psychosiques. Par L. Marchand, médecin chef de l'Asile Clinique (Ste. Anne), et A. Courtois. Préface du Dr E. Toulouse. Paper. Price, 25 francs. Pp. 144, with 31 illustrations. Paris: Librairie E. Le François, 1935.

This is an elaborate and ambitious study of 120 cases, 101 fatal, of acute, subacute and chronic psychosis, without any abnormal neurologic signs or symptoms but with inflammatory and degenerative microscopic alterations in the brain. Of the 101 fatal cases, forty-four were "primary," nineteen arose in the course of a chronic psychosis, sixteen followed the puerperium, twenty followed various infections, and two were postoperative. A state of acute delirium was present in all. Nitrogen retention was such a constant feature that the term "encéphalite azotémique" is proposed. It is admitted that this is no clinical entity, that the etiology varies and that predisposition plays an important part, but claim is made for a definite and fairly uniform histologic picture. Although one may take issue with the authors on many points, they must be given credit for originality and great industry. It is a valuable contribution to the study of the vague group of psychoses usually designated in the acute state as "acute delirium," "toxic-infectious psychosis" or "collapse delirium."

Aids to Surgery. By Cecil A. Joll, M.S., M.D., B.Sc., Senior Surgeon and Lecturer on Surgery to the Royal Free Hospital, and Reginald C. B. Ledlie, M.B., B.S., F.R.C.S., Surgeon to the Miller General Hospital. Sixth edition. Cloth. Price, $2.75. Pp. 612, with 44 illustrations. Baltimore: William Wood & Company, 1935.

This compendium represents one link in a long chain of compact booklets that cover the entire field of medicine and surgery and are especially designed to assist students in grouping and memorizing the subjects on which they are to be examined. The call for a new edition of this handsome volume proves its popularity. The work has been rewritten, enlarged and supplied with illustrations, the first of which is a tribute to American surgery, as it reproduces incisions recommended by Kanavel for the treatment of infections of the hand. The scope of the volume has restricted the authors in the main to a description of essential surgical principles and practice. Nevertheless, owing to an enviable ability to say what they want in a brief and lucid manner, the authors have succeeded in squeezing into their little book an immense amount of information. Not only the student but a general practitioner wishing to brush up his knowledge of surgical conditions will find this small volume inexpensive and extremely handy.

Thirty-Second Annual Report, 1933-1934, of the Imperial Cancer Research Fund. Under the direction of the Royal College of Physicians of London and the Royal College of Surgeons of England. Paper. Pp. 31. London, 1934.

The first part of this report gives a concise review of the content of the eleventh scientific report, which was reviewed in THE JOURNAL May 18. The most important new feature of this report is a table listing the strains of transplantable tumors maintained by the Imperial Cancer Research Fund. Twenty-eight strains are listed. The average success of grafting and the effect of reinoculation in positive animals with the same strain and with another are reported for each strain. The importance of the reinoculation behavior is understandable from the fact that it is bound up with the occurrence of spontaneous regression and the behavior of the tumors to changed environment and other conditions of growth. It was formerly

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shown by Russell and by Foulds that two distinct mechanisms may be responsible for the progressive growth of transplantable tumor strains. In some strains the parenchyma does not excite a significant degree of resistance. In the majority of progressively growing strains, however, resistance is produced but the parenchyma of the strain is insensitive to it. In such cases the presence of the resistance can be demonstrated by a reinoculation of tumor bearing animals with another sensitive strain.

Medicolegal

Hospitals: Rendition of Emergency Treatment Not Acceptance of Patient.—The regulations of the defendant hospital forbade the acceptance of patients afflicted with contagious diseases. The plaintiff took his 2½ year old daughter, desperately ill with diphtheria, to the hospital. There under direction of the house physician, Dr. Stock, the child was carried to the emergency room, a swab was made of her throat, and oxygen and 20,000 units of antitoxin were administered. A few minutes later 20,000 more units of antitoxin was administered after a consultation between Dr. Stock, the hospital superintendent and another physician. Soon thereafter the superintendent ordered the child to be removed from the hospital. Dr. Stock advised the plaintiff to obtain a physician immediately and gave him a memorandum of what had been done. The plaintiff then drove with the child about seven miles to his home. About ten minutes later the plaintiff's family physician arrived but the child died within about five minutes thereafter. The plaintiff then sued the hospital. He did not contend that the child's death was caused by failure to receive her in the hospital but that death was accelerated by the negligence of the hospital attendants, in that after receiving her and after rendering proper treatment for a while, they abandoned her when her condition demanded that she remain in bed, receive further treatment and be kept where oxygen could be given in case of heart attack. From judgment in favor of the plaintiff, the hospital appealed to the Supreme Court of Alabama.

The defendant hospital, said the Supreme Court of Alabama, was under no duty to accept the child for treatment and may have made itself liable to other patients if it had admitted her. For the plaintiff to recover, the evidence must show that the death of the child resulted from or was accelerated by the failure of the hospital to render some service which it was duty bound to render. The hospital could become duty bound to render service either (1) by undertaking to provide full hospital service or, (2) without undertaking to provide full hospital service, by rendering knowingly emergency treatment which created an extremely dangerous condition unless further partial hospital service was rendered until that hazard voluntarily created by the defendant was passed. The court was of the opinion that the evidence did not justify a finding that the defendant hospital undertook to provide any hospital service except such as may have been rendered reasonably necessary by the treatment that was given. The only fair inference to be drawn from the facts, said the court, is that the treatment given the child was but an emergency treatment. There was no evidence that the hospital undertook to provide full hospital service in violation of its regulations. To uphold the plaintiff's contention, said the court, we must assume that if the hospital did not propose to render hospital service it should have sent the child away in a desperate condition without emergency treatment, when such treatment was available and provided the only hope of recovery. The willingness of the hospital to provide such treatment should not be used to its prejudice.

Could a jury, the court asked, reasonably find that the treatment administered by the defendant accelerated her death and that careful attention at the hospital after it was given would have prolonged her life? What effect on her vitality did the antitoxin produce? The physicians who testified at the trial all agreed that a patient suffering from diphtheria should abstain from any physical exertion, whether or not antitoxin is administered. But, said the court, this requirement is not violated when the father of a small child takes her in his arms to his home in a car. None of the physicians testified that antitoxin depresses the heart. On the other hand, one physician stated that it does not have that effect. The court could find no evidence that the antitoxin created a condition which was a proximate contributing cause of the immediate death. The judgment of the lower court in favor of the plaintiff was therefore reversed and a new trial ordered.—*Birmingham Baptist Hospital v. Crews (Ala.), 157 So. 224.*

Accident Insurance: "Complete Fracture" Defined.—The defendant insurance company promised to pay certain benefits to the plaintiff "upon receipt of satisfactory proofs . . . including an x-ray photograph, indicating the complete fracture of one of the long bones of the arm. . . ." Contending that he had suffered a complete fracture of the ulna of the left arm, the plaintiff sued the insurance company. The lower court gave judgment for the insurance company, and the plaintiff appealed to the court of appeal of Louisiana, second circuit.

The question to be determined, said the court of appeal, is whether or not the injury to the ulna of the plaintiff's left arm amounted to a "complete fracture," which has been defined as "a total separation of the boneal alignment of a given bone; one in which the bone is entirely broken across." The roentgenogram of the plaintiff's injured arm, with the findings of a physician consulted by him that the fracture was complete, was sent to the defendant's home office. The roentgenogram, according to two radiologists testifying for the insurance company, revealed an incomplete fracture of the ulna. On behalf of the plaintiff, two physicians testified that they believed that the ulna was completely broken across. They stated that by manipulation of the lower arm at the situs of the injury they could hear mild crepitus, which they attributed to the broken ends of the bone grinding together, even though they found the fracture not discoverable by simple touch. Medical experts, called by the insurance company, testified that mild crepitus may be produced from an incomplete fracture, hardened tissues, ligaments and muscles. Since it was shown that roentgenograms will unquestionably reveal fractures of the bones of the arm with such clearness that experienced roentgenologists may not err in interpreting them, since roentgenologists testified that the fracture was not complete, and since, according to the evidence, crepitus may spring from causes and conditions other than a complete fracture, the court concluded that the plaintiff's physicians were mistaken in their diagnosis of the injury to the arm. Accordingly the judgment of the lower court in favor of the insurance company was affirmed.—*Meriwether v. Columbian Mut. Life Ins. Co. (La.), 157 So. 156.*

Society Proceedings

COMING MEETINGS

American Academy of Ophthalmology and Otolaryngology, Cincinnati, Sept. 14-20. Dr. William P. Wherry, 107 South 17th Street, Omaha, Executive Secretary.

American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Sky Top, Pa., Sept. 16-18. Dr. James R. Bloss, 418 Eleventh Street, Huntington, W. Va., Acting Secretary.

American Congress of Physical Therapy, Kansas City, Mo., Sept. 9-12. Dr. Nathan H. Polmer, 921 Canal Street, New Orleans, Secretary.

Colorado State Medical Society, Estes Park, September 5-7. Mr. Harvey T. Sethman, 537 Republic Building, Denver, Executive Secretary.

National Medical Association, New Orleans, Aug. 11-17. Dr. C. A. Lanon, 431 Green Street, South Brownsville, Pennsylvania, Secretary.

Northern Minnesota Medical Association, Duluth, Aug. 12-13. Dr. Oscar O. Larsen, Detroit Lakes, Secretary.

North Pacific Pediatric Society, Seattle, August 9-10. Dr. F. H. Douglass, 509 Olive Street, Seattle, Secretary.

Oregon State Medical Society, Gearhart, Sept. 19-21. Dr. Blair Holcomb, Stevens Building, Portland, Secretary.

Utah State Medical Association, Logan, September 5-7. Dr. George N. Curtis, Judge Building, Salt Lake City, Secretary.

Washington State Medical Association, Everett, Aug. 12-14. Dr. Curtis H. Thomson, 1305 Fourth Avenue, Seattle, Secretary.

Wisconsin, State Medical Society of, Milwaukee, Sept. 17-20. Mr. J. G. Crownhart, 119 East Washington Avenue, Madison, Secretary.

Wyoming State Medical Society, Lander, Aug. 12-13. Dr. Earl Whedon, 50 North Main Street, Sheridan, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to Fellows of the Association and to individual subscribers to THE JOURNAL in continental United States and Canada for a period of three days. Periodicals are available from 1925 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 12 cents if two periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

Alabama Medical Association Journal, Montgomery

4: 409-440 (June) 1935

Fracture Problems. H. E. Conwell, Birmingham.—p. 409.

Safety of Low Cesarean Section in Obstetric Emergency. T. K. McFatter, Dothan.—p. 413.

Foreign Bodies in Air and Food Passages. C. C. Perdue and G. T. Johnson, Mobile.—p. 416.

Prognosis of Pulmonary Tuberculosis. R. A. Brown, Montgomery.—p. 419.

Surgical Treatment of Pulmonary Tuberculosis. J. O. Lisenby, Atmore.—p. 422.

American J. Digestive Diseases and Nutrition, Chicago

2: 139-208 (May) 1935

Vaccine Therapy in Ulcerative Colitis: Second Part. S. Lups, Groningen, Holland, translated and edited by A. J. Baker, Grand Rapids, Mich.—p. 139.

*Hepatoptosis. C. W. McClure, H. A. Osgood and J. P. Bill, Boston.—p. 161.

Liver Function in Hepatic and Extrahepatic Diseases: II. Clinicopathologic Correlation and Evaluation of Usefulness of Liver Function Tests. G. R. Biskind, T. L. Althausen, G. K. Wever and W. J. Kerr, San Francisco.—p. 167.

Decompression of Obstructed Biliary System in the Cat: II. Serum Bilirubin Concentration and Bromsulphalein Retention. A. Cantarow, H. L. Stewart and S. G. McCool, Philadelphia.—p. 174.

Clinical Evidence of Fifty So-Called Gastro-Intestinal Diseases Which Really Are Caused by Food Allergy, with Discussion of Their Treatment. J. S. Smul, New York.—p. 178.

Diverticular Sarcoma of Stomach. J. T. Case, Chicago.—p. 185.

*Use of Duodenal Extract as an Adjuvant in Treatment of Benign Peptic Lesions: Report of Eight Cases. A. B. Rivers, Rochester, Minn.—p. 189.

The Modern Proctologic Clinic. M. J. Synnott, New York.—p. 196.

Hepatoptosis.—McClure and his associates report a case of hepatoptosis in which the positions and anatomic characters of the various intra-abdominal organs were definitely established by roentgenograms of the untreated abdomen, pyelography, barium gastro-intestinal studies and pneumoperitoneum. The exact positions of the spleen and liver were established by contrast roentgenograms after intravenous administration of a colloidal suspension of thorium dioxide. This medium permitted roentgen demonstration of the diminution in the size of the liver and the contained gummatous area resulting from antisyphilitic treatment. Fifty-three uncomplicated cases of hepatoptosis, or total displacement of the liver, have been collected from the literature and the described symptomatology has been correlated. The reported results of hepatopexy indicate that the operation is an efficient measure for relieving the symptomatology.

Duodenal Extract as an Adjuvant in Treatment of Peptic Ulcer.—The general plan of diet that Rivers used in the treatment of eight cases of benign peptic ulcer was that used by Sippy and his colleagues. Instead of gradually increasing the amount of food taken, however, this was increased rapidly, so that after four or five days the patients were taking a rather liberal diet, such as that usually given patients on ambulatory regimens. Large amounts of alkali were not used. The use of sedatives and belladonna has been continued in the belief that the treatment of ulcer is facilitated. Whenever possible, the scrupulous removal of foci of infection is advised. It is not expected that the extract of duodenal mucosa and submucosa will prove to be a specific for peptic ulcer. If some of the protecting mechanisms inherent in duodenal mucosa and submucosa could be assimilated and maintained in an extract made from these tissues, such a substance would be invaluable in the treatment of ulcer. It has not been proved whether these desirable qualities are preserved in the extract obtained from the mucosa and submucosa of the duodenum of hogs used by the author. Furthermore, such substance, when given orally, may be inert, although experimental work now being carried out gives evidence to the contrary.

American Journal of Hygiene, Baltimore

21: 249-482 (March) 1935

Effect of Atabrine and Plasmochin on Haemoproteus Infection of Pigeon. G. R. Coatney, Peru, Neb.—p. 249.

Bactericidal and Antiseptic Action of Preservatives Frequently Used in Biologic Products, and Effect of These Preservatives on Potencies of Products. Carolyn Rosenstein and Ida Levin, assisted by Hattie Levin, New York.—p. 260.

Bacterial Purification Rates in Polluted Water. J. K. Hoskins, Cincinnati.—p. 280.

Further Studies on Effect of Generally Deficient Diet on Resistance of Dogs to Hookworm Infestation. A. O. Foster and W. W. Cort, Baltimore.—p. 302.

Preparation of Antismallpox Vaccine by Culture of Virus in Chorio-Allantoic Membrane of Chick Embryos, and Its Use in Human Immunization. E. W. Goodpasture and G. J. Buddingh, assisted by Lurline Richardson and Katherine Anderson, Nashville, Tenn.—p. 319.

Studies on Benign Tertian Malaria: VIII. Observations on Splenomegaly. W. K. Stratman-Thomas, Tallahassee, Fla.—p. 361.

Id.: IX. Instance of Natural Refractoriness in Caucasian to Inoculation with Plasmodium Vivax. M. F. Boyd, W. K. Stratman-Thomas and S. F. Kitchen, Tallahassee, Fla.—p. 364.

Epizootic Fox Encephalitis: VII. Nature of Immunity. R. G. Green, N. R. Ziegler, B. B. Green, J. E. Shillinger, E. T. Dewey and W. E. Carlson, Minneapolis.—p. 366.

Mechanism of Immunity in Murine Coccidiosis. E. R. Becker, with assistance of Phoebe R. Hall and Ruth Madden, Ames, Iowa.—p. 389.

*Allergic Reactions of Actinomycetes. D. R. Mathieson, Ruth Harrison, Carolyn Hammond and A. T. Henrici, Minneapolis.—p. 405.

Studies of Endamoeba Histolytica and Other Intestinal Protozoa in Tennessee: IX. Further Observations on Pathogenicity of Certain Strains of Endamoeba Histolytica for Kittens. H. E. Meleney and W. W. Frye, Nashville, Tenn.—p. 422.

Effect of Malnutrition on Pathogenesis of Rat Leprosy. A. R. Lamb, Honolulu, Hawaiian Islands.—p. 438.

Transmission to Offspring of Immunity Against Infection with Metazoan (Cestode) Parasite. H. M. Miller Jr., St. Louis.—p. 456.

Filtrability of Bacterium Lepisepticum. Jeannette Chapman and Clara M. McKee, Baltimore.—p. 462.

Interpretation of Filtrable Viruses. R. R. Hyde, Baltimore.—p. 472.

Allergic Reactions of Actinomycetes.—Mathieson and his collaborators state that infection and immunization with acid-fast actinomycetes tend to produce an allergic sensitization in experimental animals. No cross sensitization to tuberculin could be demonstrated. Continued immunization leads to desensitization. Normal persons give more frequent and more marked skin tests to Actinomyces bovis than do actinomycotic patients. Whereas single injections of Actinomyces bovis rarely produce infection, repeated inoculations usually do. This is in agreement with the observations of Nakayama, who first suggested that allergic sensitization is a factor in the etiology of actinomycosis. No sensitization demonstrable by skin tests could be induced in rabbits inoculated with saprophytic aerobic actinomycetes. Representative actinomycetes do not elicit reactions similar to those described by Schwartzman for meningococci and other bacteria.

American Journal of Orthopsychiatry, Menasha, Wis.

5: 87-216 (April) 1935

Orthopsychiatry: Expression of Philosophy of Function. G. S. Stevenson, New York.—p. 87.

Problems of Further Research in the Rorschach Test. S. J. Beck, Boston.—p. 100.

The Rorschach Test Applied to a Group of College Students. P. L. Harriman, Lewisburg, Pa.—p. 116.

Outline of Cooperative Project for Validating the Rorschach Test. S. Rosenzweig, Worcester, Mass.—p. 121.

Introductory Remarks, Section Meeting "The Integration of Psychiatry with Education." F. L. Patry, New York.—p. 124.

Libidinal Fixations as Pedagogic Determinants. E. Liss, New York.—p. 126.

Integrating Psychiatry with the Winnetka (Illinois) Public School System. T. Burling, Winnetka, Ill.—p. 132.

*Endocrinology and Behavior Disorders of Children: Study of Possible Causal Relationships Between Endocrinopathic States and Behavior Disorders of Children. L. A. Lurie, Cincinnati.—p. 141.

Qualitative Intelligence Testing as a Means of Diagnosis in Examination of Psychopathic Children. Anni B. Weiss, Vienna, Austria.—p. 154.

Genetic Scale of Social Maturity. E. A. Doll, Vineland, N. J.—p. 180.

Endocrinology and Behavior Disorders of Children.—Lurie points out that, in evaluating the power of an endocrine disorder to produce a behavior disorder, both direct and indi-

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rect effects must be considered. The direct effects may be obvious and easily recognizable, as, for example, the mental retardation associated with cretinism or the mental deterioration that occurs in adult myxedema. On the other hand, the direct effects may be subtle and affect only the personality make up of the individual. This is often seen in cases of Froelich's dystrophy. The indirect effects are due to the emotional conflicts produced in the child as a result of his attitude to the abnormal physical condition produced by disturbance in the endocrine function. It is essential that these indirect effects be recognized, because they are often responsible for the child's inability to adjust normally to his situation in life. Approximately 20 per cent of the first 1,000 children studied at the Child Guidance Home showed various forms of glandular disturbances. In 9.3 per cent of these cases there appeared to be a direct causal relationship between the behavior disorder presented by the child and the endocrine disorder. The pituitary was most frequently involved. Mental retardation was most often associated with thyroid disturbances. No definite correlation could be established between the problem presented by the child and the endocrine involvement found to be present. Pituitary dysfunction was frequently present in all the cases of stealing. In a small group of cases, in which the problem was one of speech disturbance, there were extreme motor restlessness and destructiveness. The physical and mental development of these children was normal. All were found to be suffering from hypothyroidism. Seventy-one of the children in the series received glandular therapy. In 33 per cent the results were good, in 50 per cent fair and in 17 per cent poor. Endocrine disturbances cannot all be corrected by glandular therapy. This is especially true of glandular overactivity. Glandular therapy, like all other forms of therapy, to be successful, must be based on correct diagnosis.

American Journal of Pathology, Boston

11: 373-590 (May) 1935

Cystic Disease of Kidneys. E. T. Bell, Minneapolis.—p. 373.
Lipid Content of Livers of Nonimmunized and Immunized Horses. A. Wadsworth, L. W. Hyman and R. R. Nichols, Albany, N. Y.—p. 419.
Ganglioneuroma in Neck of Child. J. McFarland and S. W. Sappington, Philadelphia.—p. 429.
Primary Carcinoma of Lung: Pathologic Study. K. B. Olson, Boston. —p. 449.
*Histologic Effects of Potassium Iodide and Thyroid Substance on Thyroid Gland of Guinea-Pig in Experimental Scurvy. W. F. Abercrombie, New York.—p. 469.
Glomerular Changes in Arteriosclerotic Contraction of Kidney. P. Kimmelstiel, Boston.—p. 483.
Reaction of Pulmonary Tissue to Lipiodol. R. D. Wright, Melbourne, Australia.—p. 497.
Infarction of the Liver. I. J. Pass, Minneapolis.—p. 503.
Primary Adenocarcinoma of Pancreas in Fifteen Year Old Boy. P. A. Mielcarek, Cleveland.—p. 527.
*Basophilic Degeneration of Heart Muscle. Maria E. Haumeder, Rochester, Minn.—p. 535.
Adeno-Acanthoma of Pylorus. J. G. Pasternack, Washington, D. C.—p. 541.
Erythroblastosis: Report of Case Presenting Erythroblastic Tumor in Thoracic Cavity. G. W. Covey, Lincoln, Neb.—p. 551.
Alteration in Serum Bilirubin and Bromsulphalein Retention in Relation to Morphologic Changes in Liver and Bile Passages in Cats with Total Biliary Stasis. A. Cantarow and H. L. Stewart, Philadelphia. —p. 561.
Siderotic Nodules (Gandy-Gamna Bodies) in Primary Renal Carcinoma. D. R. Morgan, M. M. Lieber and H. L. Stewart, Philadelphia.—p. 583.

Experimental Scurvy.—Abercrombie observed that the thyroids of guinea-pigs in scurvy present irregular follicles with higher epithelium, a reduced amount of nonuniformly stained but extensively vacuolated colloid and an increase in the interfollicular cells. These changes are more marked in chronic scurvy of long duration than in acute scurvy. Potassium iodide, when administered to animals with scurvy, causes a decrease in the number of vacuoles and an increase in the amount of the colloid, accompanied by a flattening of the epithelium and a decrease of the interfollicular cells. Thyroid substance produces similar results, except that the epithelium is not flattened but is returned to the normal medium height. Potassium iodide and thyroid substance, in the doses administered, do not tend to prolong the life of the animal in experimental scurvy. Thus, it appears that vitamin C is not concerned with iodine metabolism.

Basophilic Degeneration of Heart Muscle.—In a study of 320 consecutive postmortem examinations of sections of the heart obtained by routine procedure, Haumeder found the lesion (basophilic degeneration) described by Hewitt in 107. The areas of degeneration were of microscopic size. It is her impression that the degeneration passes through several phases. With the hematoxylin and eosin stain, the degenerated portions were seen as basophilic patches that generally occupied the centers of the muscle bundles and frequently included the well preserved, often hypertrophied, nucleus. They always were of well defined limits and at the periphery of each was a zone of normal muscle tissue. No tissue reaction could be seen in the degenerated areas. The normal structure was preserved in the immediate neighborhood and even in the continuation of the involved muscle bundle. No gross change in the heart muscle could be observed. In the early stage of the process these degenerated areas stained a rather dark blue and were fairly dense, finely granular and occasionally clumped, and sometimes included fragments of muscle fibers. As the process advanced these areas stained a lighter blue, and what was apparently vacuolization appeared. In advanced stages there was left only a fine network of basophilic, intertwining fibers, which included small tissue spaces, the lesion being rather indistinct. The most frequent single site of the lesion was the septum. Closely following this in frequency was the left ventricle; the right ventricle showed fewer lesions. Of the cases in which the lesion was found in more than one site, those in which the septum and left ventricle were involved were the most numerous. The lesion was found only five times in the right ventricle alone and was found in combination in the right ventricle and septum only twice. In order to ascertain the nature of the lesion, several differentiating stains were used. The lesion was found most frequently in cases of malignancy and heart disease. It was also found in many cases of infection and inflammation, as well as in single cases of electrocution, drowning and toxemia from burns. Staining reactions showed that the areas contained mucin as well as a component related to glycogen.

American Journal of Surgery, New York

28: 531-854 (June) 1935

*Technic of Operation on Common Bile Duct, with Especial Reference to Instrumental Dilatation of Papilla of Vater. A. W. Allen and R. H. Wallace, Boston.—p. 533.
Stricture of Common Bile Duct: Report of Case. K. H. Aynesworth, Waco, Texas.—p. 562.
Unusual Tumor (Malignant Adenoma) of Liver in Baby. F. W. McRae, Atlanta, Ga.—p. 575.
Surgical Emergencies During Pregnancy. W. F. Shallenberger, Atlanta, Ga.—p. 582.
Total versus Subtotal Abdominal Hysterectomy in Benign Uterine Disease. E. H. Richardson, Baltimore.—p. 588.
Injuries Peculiar to Modern Football. L. H. Landry, New Orleans.—p. 601.
*Suppurative Pericarditis. G. H. Bunch, Columbia, S. C.—p. 613.
Coronary Occlusion Simulating an Acute Abdominal Emergency. J. M. T. Finney Jr. and C. F. Mohr, Baltimore.—p. 629.
Postoperative Thrombosis and Embolism. F. W. Bancroft, Margaret Stanley-Brown and A. J. Quick, New York.—p. 648.
*Scalenus Anticus (Naffziger) Syndrome. A. Ochsner, Mims Gage and M. DeBakey, New Orleans.—p. 669.
Aneurysm of Temporal Artery: Analysis of Cases Reported in Literature to June 1, 1934, and Report of Case of Traumatic Origin. N. Winslow and M. Edwards, Baltimore.—p. 696.
Right Paraduodenal Hernia. R. C. Bryan, Richmond, Va.—p. 703.
Pseudomyxoma Peritonei: Report of Case Presenting Bronchial Fistula. J. D. Hancock and H. M. Weeter, Louisville, Ky.—p. 731.
Some Observations on Treatment and After-Care of Fractured Bones. E. D. Newell, Chattanooga, Tenn.—p. 742.
Problems in Treatment of Fractures of Long Bones. E. L. Gilcreest, San Francisco.—p. 754.
*Malignant Changes in So-Called Benign Giant Cell Tumor. W. B. Coley, New York.—p. 768.
Added Problems Presented by Gas Gangrene and Tetanus in Compound Fractures. R. G. Carothers, Cincinnati.—p. 821.
Ovarian Thyroid. R. L. Sanders, Memphis, Tenn.—p. 831.
Other Laboratory Methods in the Handling of Thyroid Disease. G. D. Mahon Jr., Dallas, Texas.—p. 841.

Operation on Common Bile Duct.—Allen and Wallace incorporate some points of the technic of Cheever and Bakeš and certain details advocated by others in the development of a more or less routine management of the operation on the common bile duct, which is given. The indications for exploration of the common bile duct are given. Routine dilation of the papilla of Vater in surgery of the common duct and

temporary external drainage of the duct by catheter are advocated. Some experimental and considerable clinical evidence is presented showing that dilation of the papilla of Vater can be carried out with safety. It is probable that dilatation of the outlet of the pathologically distended common bile duct may last some time. It would appear that dilatation of the normal papilla in dogs is not permanent.

Suppurative Pericarditis.—Bunch believes that the incidence of the disease is much greater than indicated by the less than 200 operative cases reported in the literature. This is borne out by Brooks, who in necropsies done in 200 consecutive cases of pneumonia found seventy-five with positive blood cultures or pathologic signs of septicemia and not one with purulent pericarditis. Nontraumatic suppurative pericarditis is essentially secondary and most frequently follows respiratory disease, particularly pneumonia, septicemia, rheumatic fever and osteomyelitis. The symptoms of pyopericardium are those of sepsis and impaired circulation from mechanical embarrassment of heart action due to increasing pressure made on the heart by the accumulating effusion. When infection of the pericardium occurs, there is apt to be precordial pain with exacerbation of septic symptoms already present. There is more often, however, continuation of symptoms in a patient who is obviously not doing well. There may be chills with high fever. The dyspnea may be extreme. The diagnosis of pyopericardium remains a challenge to the profession, for effective treatment depends on early recognition. Symptoms are only suggestive, but physical signs are characteristic. In spite of the nominal danger of puncturing the heart or of injuring the coronary vessels with the needle, careful paracentesis is indicated in effusion to determine the character of the fluid. Roentgen examination of the chest should always be made. Pericardial effusion is present when there is an enlarged area of precordial dulness shifting with change of position and when roentgen examination shows a water bottle shadow with the base below. The mortality of purulent pericarditis treated medically is practically 100 per cent. Although suppurative pericarditis most often follows pneumonia, there may be other complications of the disease, notably empyema. Winslow and Shipley state that in the 128 cases reviewed by them empyema was diagnosed and drained in sixteen patients, seven of whom recovered and nine died following thoracotomy. The treatment of suppurative pericarditis is adequate dependent drainage by open operation as soon as the diagnosis is made. After pericardiotomy, if septic symptoms continue or return after improvement has begun, an encapsulated pus pocket should be sought for in the posterior pericardium or in the pleura. Left undrained, such a pocket will result in death. After recovery, many patients have normal function of the heart. The author has confirmed this in his two cases by physical and roentgen examination and by electrocardiographic study.

Scalenus Anticus Syndrome.—Ochsner and his associates point out that the scalenus anticus syndrome is a clinical entity the symptoms of which are identical with those of cervical rib. The symptoms are the result of compression of the brachial plexus and subclavian artery on the first thoracic rib. This compression may be due to an abnormally low position of the shoulder, high fixation of the sternum and ribs, low origin of the brachial plexus and elevation of the first thoracic rib due to spasm of the scalenus muscles, resulting from brachial plexus irritation. The first three conditions are predisposing, whereas the last is an exciting factor. Irritation and stimulation of the brachial plexus by pressure of the first rib causing spasm and shortening of the scalenus anticus muscle result in elevation of the first rib, thus establishing a vicious circle. Vascular changes are frequently present but are usually missed unless oscillometric studies are made. The scalenus anticus syndrome must be differentiated from the cervical rib syndrome, subacromial bursitis, supraspinatus tendon rupture, cervicodorsal sympathalgia, Raynaud's disease and brachial plexus neuritis. The treatment consists of resection of a portion of the scalenus anticus muscle. Six cases of scalenus anticus syndrome, with successful operation in four, are reported.

Malignant Changes in So-Called Benign Giant Cell Tumor.—Coley is still of the opinion that giant cell sarcoma is always benign and never gives rise to metastases. While some of the cases reported as benign giant cell tumors that later become malignant may be best explained as errors in diagnosis, there is a considerable number in which the evidence indicates that the primary tumor was a true benign giant cell tumor which later, because of some unknown cause, changed in character to a malignant metastasizing tumor. This distinction is really only academic. The proportion of cases in which tumors diagnosed as benign giant cell tumor by experienced pathologists have later become malignant, although small, is actually much larger than has been recognized by recent writers. It is probably in the neighborhood of 15 per cent. The acknowledgment of the fact that a considerable number of giant cell tumors do later become malignant should not lead one to abandon conservative methods of treatment for more radical measures (amputation). It should increase the efforts to arrive at a correct diagnosis at the earliest possible moment. The patient with an apparently cured giant cell tumor should be cautioned to avoid any local trauma. The fact that such a high percentage of the author's series of malignant giant cell tumors were treated by irradiation (radium or x-rays) after curettage suggests that this mode of treatment should be abandoned. If irradiation is the method of choice, it should be used alone and not in conjunction with curettage. He concludes that surgery (curettage, chemical cauterization, without packing or drainage), with or without postoperative toxin treatment, offers the greatest proportion of permanent cures with the shortest period of disability and the least impairment of function. A brief period of postoperative toxin treatment (from four to six weeks) will lessen the number of recurrences. The fact that such a considerable number of cases diagnosed as benign giant cell tumor have later become malignant leads one to ask whether the use of the term benign giant cell tumor should be continued or whether a return should be made to the older classification of giant cell sarcoma.

American Review of Tuberculosis, New York

31: 601-714 (June) 1935

*Dust and Its Relation to Tuberculosis. J. B. Hawes 2d, Boston.—p. 601.

Further Studies on Pathologic Significance of Leukocytic Reaction in Tuberculosis: I. Presentation of Leukocytic Index with Calculator to Facilitate Its Computation. A. M. Crawford, Mount McGregor, N. Y.—p. 611.

Id.: II. Presentation of Pathologic Concept Through Use of Leukocytic Index in Selected Groups of Tuberculous Cases. E. M. Medlar, Mount McGregor, N. Y.—p. 621.

Id.: III. Comparison of Leukocytic Reactions as Found With and Without Artificial Pneumothorax Therapy. E. M. Medlar, Mount McGregor, N. Y.—p. 628.

Id.: IV. Test of Validity of Pathologic Interpretation Placed on Leukocytic Reaction. E. M. Medlar, Mount McGregor, N. Y.—p. 642.

Cavities in Pulmonary Tuberculosis: Their Relation to Mortality Rate and Duration of Life. S. E. Simpson, Rochester, N. Y.—p. 658.

Treatment of Pulmonary Tuberculosis by Hyperpyrexia: III. Temperatures That Inhibit Growth of Cultures of Mammalian and Avian Tubercle Bacilli and One Strain of Leprae Bacillus: Method of Typing Suggested. G. R. Duncan and E. S. Mariette, Oak Terrace, Minn.—p. 687.

The Tuberculosis Problem. L. J. Moorman, Oklahoma City.—p. 698.

Relation of Dust to Tuberculosis.—Hawes believes that exposure to protein dusts, some of which may occasionally cause asthma, hay fever or other anaphylactic phenomena, to the carbohydrate dusts, such as flour, which presumably have no effect, specific, irritating or otherwise, and to the inorganic non-silicon-containing dusts, including lime, marble, carbon and other elements, in normal amounts and under normal conditions will not reactivate an arrested or quiescent tuberculous process. He does believe, however, that dust in excessive amounts under abnormal conditions, such as street dust in winter and fall or germ laden dust from sleeping cars, which might well cause irritation and infection of throat, trachea and bronchi, is a potential source of harm. Dust that may cause allergic phenomena, such as asthma, asthmatic bronchitis or hay fever, will not reactivate or harm a tuberculous process. As to allowing an arrested or quiescent tuberculous patient to take up a trade in which he would be exposed to a harmless dust, the author would be quite willing to allow his patients to take up such dusty work unless the conditions as to dust were extremely bad.

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Anatomical Record, Philadelphia

62: 109-212 (May 25) 1935

Study of Seasonal Changes in Thyroid Gland of Thirteen-Lined Ground Squirrel (Citellus Tridecemlineatus), with Particular Reference to Its Sexual Cycle. M. Zalesky, Chicago.—p. 109.
Variations in Arrangement of Branches Arising from Aortic Arch in American Whites and Negroes: Second Study. G. D. Williams and H. W. Edmonds, St. Louis.—p. 139.
*Nature of Pulmonary Alveolar Lining. L. E. Josselyn, Chicago.—p. 147.
Congenital Absence of Tibia. J. Dankmeijer, Amsterdam, the Netherlands.—p. 179.
Extra-Ovarial Sex Cords on Armadillo Ovary. G. W. D. Hamlett, Boston.—p. 195.
Effects of Antuitrin S and Pituitary Extract on Armadillo Ovary. G. W. D. Hamlett, Boston.—p. 201.

Nature of Pulmonary Alveolar Lining.—Josselyn states that the black lines seen on alveolar septums in silver nitrate impregnations of lungs are explainable otherwise than by the view that characterizes them as outlines of lining epithelial cells. The occasional nuclei seen in alveolar walls in addition to those of the capillary endothelium belong to histiocytes and possibly other connective tissue cells. The phagocytic cells that occur in such profusion in the alveoli in case of need are histiocytes and of largely extraneous origin. The alveolar walls, in addition to the capillary vessels and cells, consist of a membrane composed of reticular and elastic fibers and a homogeneous transparent ground substance. It is on the latter that the continuity of the membrane depends. Alveolar pores are seen sparsely in young adult lungs fixed while inflated with air. They are more frequent in older animals and in those whose lungs were fixed by the intratracheal introduction of fluid. They thus appear to owe their existence to the traumas of everyday life as well as to those of fixation.

Annals of Surgery, Philadelphia

101: 1299-1468 (June) 1935

Adenoma of Islet Cells with Hyperinsulinism: Review. A. O. Whipple and Virginia Kneeland Frantz, New York.—p. 1299.
*Subtotal Pancreatectomy for Hyperinsulinism: Operative Technic. J. M. McCaughan, St. Louis.—p. 1336.
Surgical Treatment of Chronic Pancreatitis. G. De Tarnowsky and P. J. Sarma, Chicago.—p. 1342.
Superior Laryngeal Nerve and Superior Pole in Thyroidectomies. C. H. Frazier and W. H. Erb, Philadelphia.—p. 1353.
Surgical Treatment of Toxic Goiter. M. K. Smith, New York.—p. 1358.
Traumatic Intrathoracic Rupture of Thoracic Duct with Chylothorax: Report of Case with Recovery. O. R. Lillie and G. W. Fox, Milwaukee.—p. 1367.
*Surgical Aspects of Bleeding Gastric and Duodenal Ulcer. J. J. Westermann, New York.—p. 1377.
Spontaneous Rupture of Normal Spleen. R. H. Young, New York.—p. 1389.
Gas Gangrene: Review of Seventeen Cases. E. Eliot Jr. and E. R. Easton, New York.—p. 1393.
Carcinoma of Bladder. C. R. O'Crowley, Newark, N. J.—p. 1407.
Surgery of Bladder Tumors. E. Beer, New York.—p. 1412.
Total Cystectomy for Cancer of Bladder. W. C. Quinby, Boston.—p. 1415.
*Diathermy for Carcinoma of Bladder. V. S. Counseller and W. F. Braasch, Rochester, Minn.—p. 1418.
Radium Treatment of Cancer of Bladder. B. S. Barringer, New York.—p. 1425.
Treatment of Bladder Cancer with External Irradiation. A. L. Dean Jr., New York.—p. 1428.
Upper Urinary Tract in Carcinoma of Bladder. J. R. Caulk, St. Louis.—p. 1432.

Subtotal Pancreatectomy for Hyperinsulinism.—In McCaughan's experience the following technic has simplified subtotal pancreatectomy: Shortly before operation the patient is given 500 cc. of a 10 per cent solution of dextrose intravenously, and the stomach is thoroughly emptied of fluid and gas by aspiration. The preliminary medication consists of one-sixth grain (0.01 Gm.) of morphine sulphate and 1/150 grain (0.0004 Gm.) of atropine sulphate given hypodermically. Ether anesthesia is used by preference because of its effect in sustaining and even elevating the normal level of the blood sugar. A long left midrectus incision is made. The gastrocolic omentum is divided transversely and a gauze pack is placed against the stomach, which is rotated slightly and drawn upward by an assistant. A second pack is placed over the transverse colon, which is then displaced downward. The small of the back is elevated by means of the operating table backrest. The resection is begun by dividing the peritoneal investment along the lower margin of the pancreas and grasping the tail with a suitable forceps and drawing it slightly forward and downward. Temporary tape ligatures are passed about the splenic vein and splenic artery. The subsequent dissection is directed toward the freeing of the tail and the body of the pancreas from the splenic artery and vein, because it not only enables one by traction and countertraction to display the numerous tributary vessels supplying the tail and body of the pancreas by placing them on a stretch but it also gives immediate control of the vascular pedicle of the spleen should either vein or artery be inadvertently wounded. The tributary vessels may be divided between ligatures, either an aneurysm needle or an artery forceps being used to introduce the suture underneath the vessel. The large pancreatic artery should be secured early in the dissection. The dissection is continued until the region of the junction of the body with the head is reached. As much of the gland is removed as seems indicated by the severity of the case at hand. An assistant holds the body of the pancreas in the grasp of a rubber covered right angle forceps, just tightly enough to control bleeding. The pancreas may then be divided with a V type incision and the stump closed with either an interrupted mattress suture or running lock stitch, giving satisfactory hemostasis. A rubber tissue drain is introduced to the bed of the resected portion and the gastrocolic omentum is closed loosely about the drain. After operation the blood sugar should be maintained at normal levels by the administration of carbohydrates.

Surgical Aspects of Bleeding Gastric Ulcer.—Westermann states that of the cases of gastroduodenal ulcer seen at the hospital during the past ten years about 12 per cent have been complicated by hemorrhage. In 75 per cent of these cases the hemorrhage has been massive and recurrent. In every case transfusion has been given at least once, and frequently more often, either during the course of a medical regimen or as a preoperative or postoperative measure. These records show that transfusion has been completely ineffectual as a means of stopping hemorrhage. The advisability of operation during the hemorrhage is debatable. However, hemorrhage of such proportions elsewhere in the body is always treated as a surgical emergency. Patients operated on under these circumstances have survived. One immediate death occurred in a case complicated by carcinoma of the pancreas. In each instance in which the operation performed was of the indirect type the hemorrhage continued. Westermann is of the opinion that immediate surgery of the direct type is justifiable in a large percentage of these cases and will prove permanently successful. The presence of the lesion can be determined only by careful inspection at operation with the duodenum open. Preoperative and postoperative transfusions are an absolute requirement of this procedure. Ten patients in this series died in the hospital from continued hemorrhage while receiving most rigid medical treatment and, in many instances, daily transfusions. The source of massive hemorrhage that complicates gastroduodenal ulcer is from the posterior surface of the duodenum in a large majority of cases. The blood supply of this area makes gross hemorrhage possible without deep penetration of the wall. Exploration of the open duodenum is necessary to determine this source in all cases except those in which there are large penetrating ulcers of the crater type. Preoperative diagnosis is usually definite in these cases, but diagnosis of the posterior surface ulcer is extremely difficult and cannot be accurate.

Diathermy for Carcinoma of Bladder.—Counseller and Braasch point out that the use of diathermy in the surgical management of carcinoma of the bladder is gradually being extended, for it has brought within the field of successful treatment cases in which the condition formerly would have been regarded as inoperable or the growth as nonresectable. Seventeen patients whose condition was considered inoperable were treated extensively with diathermy alone, and fifteen of the seventeen lived more than five years. The two others have recently died from unrelated conditions. Tumors of the bladder that are comparatively small and are of a malignancy graded 1 or 2 are usually controlled by transurethral electrocoagulation. Some of the early circumscribed lesions that are graded 3 or 4 and that can be seen easily and give no clinical

evidence of infiltration may be treated similarly. The more extensive, highly malignant lesions and the widespread lesions with low degrees of malignancy are attacked preferably by the suprapubic route. Whenever the lesion can be completely removed surgically by either segmental resection or excision, this is the operation of choice. For the inoperable lesions of both high and low grades, confined to the base, electrocoagulation is used. The small number of recurrences and the lack of deformity and infection of the bladder would recommend this method of treatment. In some instances these procedures may be combined with the application of radon seeds or of needles containing radium. The advantages of diathermy as a transvesical procedure for inoperable or nonresectable lesions of both high and low grades have not been sufficiently recognized.

Archives of Dermatology and Syphilology, Chicago

31: 777-938 (June) 1935

Reactions Due to Phenolphthalein: Study of Their Pathogenesis. E. W. Abramowitz, New York.—p. 777.

Study of Crude Coal Tar and Allied Substances: Preliminary Report. M. E. Obermayer and S. W. Becker, Chicago.—p. 796.

*The Arsenic Problem: Report of Case of Probable Arsenic Dermatitis from Wearing Apparel. M. J. Reuter, Milwaukee.—p. 811.

Reactions to Trichophytin Compared with Reactions to Other Bacterial Products. H. Goodman and I. Marks, New York.—p. 819.

*Acne and Furunculosis: Preliminary Report of Treatment with Physiologic Solution of Sodium Chloride Locally or by Intravenous Injection. H. Goodman, New York.—p. 828.

Experimental Chronic Cutaneous Blastomycosis in Monkeys: Study of Etiologic Agent. W. A. DeMonbreun, Nashville, Tenn.—p. 831.

Congenital Defect of Skin of the New-Born. R. L. Sutton Jr., Kansas City, Mo.—p. 855.

Nonulcerative Tuberculosis of Mouth Following Dental Procedure: Report of Case. C. R. Rein and M. H. Feldman, New York.—p. 858.

New Syphilitic Dental Dystrophy (Similar to the Bud Molar of Pflüger). E. W. Karcher, Boston.—p. 861.

The Arsenic Problem.—Reuter cites a probable case of arsenical dermatitis caused by wearing a black woolen suit. Arsenic was found in the urine and hair of the patient and in the suit. Recovery occurred when the patient discontinued wearing the suit and when local treatment of the skin was instituted. The presence of arsenic in excretions is discussed. There are no definite criteria by which to identify arsenic as a cause of disease in a given case. At present the diagnosis in obscure cases of arsenical poisoning rests on presumptive evidence. A general rule regarding the behavior of arsenic within the body is of little value, because in many persons the biochemical reactions are exceptional. Patients who suffer from symptoms of arsenic poisoning are exceptions in that they manifest a hypersensitivity to arsenic. Legally, it is difficult to state whether or not arsenical poisoning has been the cause of death, even though the amounts of arsenic found in the tissues and excretions are the same or less than those cited as "normal" values. The use of arsenic as a contaminating factor in foods or drugs should not be permitted, since no limit of tolerance for arsenic can be established for all persons.

Treatment of Acne and Furunculosis.—Goodman studied the effect of intravenous and local injection of physiologic solution of sodium chloride for the relief of pustular acne and furunculosis, treating several hundred patients. The pustular elements have always receded under this type of treatment. The large pus pockets of the condition sometimes called cystic acne have cleared and remained clear. Furuncles likewise are amenable to this form of therapy. It seems to make no difference whether the furuncle is in the frank pustular phase or in the stage before ripening. The first injection was 100 cc., which was increased by 50 cc. until a maximum of 250 cc. was reached. A few patients were given 300 cc. There were no ill effects. The injections were carried out by the gravity method. If the patient had only one or two pus pockets, the solution was injected locally, directly into the mass of pus. Injections were made around the inflammatory base as well. The amount varied with the quantity that could be injected. If there was an aperture in the pustule, the solution acted as a means of irrigation. Recently Bloom reported excellent results in the treatment of certain skin conditions, including acne, from the use of calcium chloride intravenously. Patients with pustular acne were relieved of the pus pimples when given intravenous injections of physiologic solution for such unrelated conditions as vascular diseases of the lower extremities. The relation of a high sugar content to a low salt content may be found to be constant for infections. Persons with frank diabetes are prone to have pustular infections of the skin. Intravenous injections of physiologic solution of sodium chloride may be indicated in such cases.

Archives of Surgery, Chicago

30: 911-1084 (June) 1935

*Tumor of Neuromyo-Arterial Glomus: Report of Cases. V. Raisman and L. Mayer, New York.—p. 911.

Otogenous Abscess of Parietal Lobe: Review of Literature and Report of Six Cases C. B. Courville and J. M. Nielsen, Los Angeles.—p. 930.

Diagnosis of Neurogenic Lesions of Urinary Bladder by Cystometry: Appraisal of Method Based on Experimentation with Animals. J. M. McCaughan and J. H. Hershey, St. Louis.—p. 956.

*Vaso-Orchidostomy with Interposed Spermatocele: Procedure for Treatment of Sterility. S. F. Wilhelm, New York.—p. 967.

Melanosis Coli: Its Clinical Significance. A. J. Zobel and D. A. Susnow, San Francisco.—p. 974.

*Gangrene of Buttock, Perineum and Scrotum Due to Endamoeba Histolytica: Report of Case. F. L. Meleney, New York, and H. E. Meleney, Nashville, Tenn.—p. 980.

Lumbar Vertebral Epiphysitis. S. Kleinberg, New York.—p. 991.

Surgical Treatment of Ependymal Glioma of Spinal Cord. L. J. Adelstein and G. H. Patterson, Los Angeles.—p. 997.

Use of Low Temperatures in Culture and Transportation of Surgical Maggots. S. W. Simmons, Washington, D. C.—p. 1015.

Adequacy of Nutritional Retardation in Culture of Sterile Maggots for Surgical Use. S. W. Simmons, Washington, D. C.—p. 1024.

Peritoneal Drainage: Resistance of Sinus Tract to Infection. P. Shambaugh and R. Boggs, Boston.—p. 1032.

Penetration of Moist Heat Applied to Abdomen and Its Effect on Intestinal Movements. H. E. Carlson and T. G. Orr, Kansas City, Kan.—p. 1036.

*Suction with Nasal Catheter: Its Effect on Blood Chemistry: Report of Case. R. F. Northrop, Philadelphia.—p. 1040.

Acute Pancreatitis. F. F. Henderson and E. S. A. King, Boston.—p 1049.

Review of Urologic Surgery. A. J. Scholl, Los Angeles; E. S. Judd, Rochester, Minn.; J. Verbrugge, Antwerp, Belgium; A. B. Hepler, Seattle; R. Gutierrez, New York, and V. J. O'Conor, Chicago.—p. 1058.

Glomal Tumor.—Raisman and Mayer add three cases of glomal tumor to the twenty-six cases previously reported. This benign tumor develops from a structure normally present in the skin and known as the glomus. It is probably identical with the "painful subcutaneous nodule" reported by Wood in 1812, referred to by others. The authors collected thirty-three instances of "probable but unproved cases of glomal tumor." The glomal tumor is small, usually not more than half an inch (1.27 cm.) in diameter, of slow growth and long duration. It may be situated in any part of the body, but the favorite site is beneath the nail. There it gives rise to pain of varying intensity and radiation. In the severe cases the pain in agonizing, almost paroxysmal, and radiates upward to the shoulder, even to the heart. When the tumor is not subungual, the pain is usually much less severe. Changes of temperature, particularly cold, increase the severity of the pain. Invariably the tumor is sensitive to pressure. In some cases it is associated with neurologic or vascular changes, such as hyperesthesia and increase in the temperature of the skin. In two cases there was slight atrophy of the entire arm. Examination reveals a pea-sized tender tumor, which, when subungual, has almost always a peculiar bluish tinge showing through the translucent nail. A roentgenogram may show a minute crater-like depression of the dorsal cortex of the terminal phalanx. The only effective treatment is excision by knife or by endothermy. If the tumor is subungual, exposure is secured by removal of a portion of the nail, which in many cases regenerates normally. The tumor may be encapsulated as in the majority of cases, or diffuse as in one of the present cases. No metastases or recurrences after excision have been reported. Invariably pain has disappeared after removal of the tumor. Glomal tumor is easily differentiated from most of the cutaneous neoplasms. Only the unusual single small neuroma, superficially located, and the subungual melanoblastoma may cause difficulty. This extremely malignant tumor at one phase of its development is characterized by a bluish black spot beneath the nail which might be mistaken for a glomus. Operation and microscopic section will at once make the differential diagnosis possible.

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Vaso-Orchidostomy with Interposed Spermatocele.—Wilhelm has devised a procedure for vaso-orchidostomy that entails the creation of an artificial spermatocele, which he believes will increase the percentage of success of operations to reestablish the seminiferous channels and more nearly reproduces the normal anatomic conditions. The entire spermatogenic tissue should be used. The testicle should not be damaged. The site of the anastomosis should be completely epithelial, so that a minimum of scar is formed. A funnel-shaped sac lined with epithelium, analogous to a spermatocele, should be established to unite the larger cut open surface of the tubules of the epididymis or of the rete to the smaller divided end of the vas deferens. Following experiments on animals, the operation for the reestablishment of the seminiferous channels was carried out in two stages. The first stage consisted of permanent vasostomy. After complete healing had taken place, the second stage, vasosac orchidostomy, was performed.

Gangrene of Buttock and Perineum Due to Endamoeba Histolytica.—The Meleneys discuss a case of gangrene of the buttocks, perineum and scrotum from the clinical, bacteriologic and pathologic standpoints, and reach the conclusion that it was due primarily to the lytic action of Endamoeba histolytica. This case has been studied carefully with anaerobic bacteriologic technic, thus ruling out the presence of the microaerophilic nonhemolytic streptococcus, which is the essential organism in the progressive postoperative synergistic gangrene with which this disease might be confused. The patient made a rapid recovery following the complete excision of the lesion, the administration of a course of chiniofon and emetine hydrochloride, the local application of zinc peroxide and the application of skin grafts. In this case there was relatively little gangrene of the skin and the line of demarcation was relatively smooth and sharply outlined, the margin of skin outside the gangrene was not raised, there was no red zone and the wound was not extremely tender. The margin of the skin elsewhere was extensively undermined and the granulating base of the ulcer was rough and shaggy with necrotic tissue adherent to it. Although the clinical appearance of the lesion was quite different from that seen in cases of postoperative synergistic gangrene, other cases of amebic ulceration of the skin may not be so distinctive in their clinical appearance. In some cases of bacterial gangrene, amebas may be present as contaminating organisms without taking part in the gangrenous process. In other cases both factors may operate and change the characteristic clinical picture accordingly. The bacteriologic study confirmed this differentiation, for in the synergistic type of gangrene the essential organism, a micro-aerophilic nonhemolytic streptococcus, may always be found in pure culture of material from the area just outside the margin of the gangrene and is associated with Staphylococcus aureus in the gangrene. The nonhemolytic streptococcus was cultivated only from material in the zone outside the gangrene. The amebas were found in the advanced zone of infection, while the bacteria were in the rear.

Effect on Blood Chemistry of Continuous Suction with Nasal Catheter.—Northrop studied the effect of continuous drainage of the stomach and duodenum through a nasal catheter in twenty-five patients, twenty-four of whom were operated on. Continuous suction applied through a nasal catheter causes a drop in the blood chlorides, an elevation of the carbon dioxide-combining power toward or into alkalosis, an elevation of the hemoglobin content of the blood and an increase in the red blood cell count. The marked changes in the chlorides, hemoglobin and red cell content of the blood and the changed carbon dioxide-combining power accompanying continuous lavage of the upper intestinal tract produce few, if any, untoward symptoms. Of the various methods of administering para-oral fluids, continuous venoclysis appears to be most effective in controlling the changes in the blood incident to continuous duodenal suction. Administration of the aspirated intestinal contents in the form of retention enemas does not cause rectal irritation and deserves further study as a means of combating postoperative dehydration and the loss in chlorides and the alkalosis incident to obstruction of the intestine and continuous lavage of the stomach. The use of a properly functioning nasal catheter with applied suction is an efficient way of controlling postoperative nausea, vomiting and distention and should be used prophylactically in cases in which this triad is anticipated. A case of obstruction of the intestine with recovery under duodenal suction is reported.

California and Western Medicine, San Francisco

42: 409-496 (June) 1935

Organized Medicine in California: Some of Its Problems. C. G. Toland, Los Angeles.—p. 409.
Research in Medicine: Practical Applications. E. S. Judd and M. T. Hoerner, Rochester, Minn.—p. 412.
Differential Diagnosis of Intracranial Damage. E. J. Morrissey, San Francisco.—p. 416.
Urethral Strictures: Résumé of Treatment. W. B. Parker and C. H. MacKay, Los Angeles.—p. 421.
Mussel Poisoning. H. Sommer and K. F. Meyer, San Francisco.—p. 423.
Sight Saving Classes. F. H. Rodin, San Francisco.—p. 426.
Encephalography in Children. F. G. Lindemulder, San Diego.—p. 429.
Reconstructive Plastic and Oral Surgery. A. E. Smith, Los Angeles.—p. 432.
Surgical Relaxation. J. R. Burrows, San Francisco.—p. 438.
Common Dermatoses: Some Unusual Manifestations. N. P. Anderson and S. Ayres Jr., Los Angeles.—p. 442.
Health Insurance: Pro and Con: Being Speeches Made at the Special Session of the House of Delegates of the California Medical Association at Los Angeles, March 2-3, 1935. Remarks by R. A. Yoell, San Francisco; J. H. Shephard, San Jose; A. R. Kilgore, San Francisco; D. R. Powell, Stockton; D. Crosby, Oakland; N. G. Hale, Sacramento; H. Wilson, Los Angeles; C. A. Broaddus, Stockton; L. A. Packard, Bakersfield; J. C. Ruddock, Los Angeles; T. C. Lawson, Oakland, and C. M. Anderson, Hermosa Beach.—p. 445.

Canadian Medical Association Journal, Montreal

32: 609-724 (June) 1935

Observations on Treatment of Dysmenorrhea with Placental Extract "Emmenin." M. C. Watson, Toronto.—p. 609.
*Treatment of Menorrhagia and Metrorrhagia by Anterior Pituitary-Like Hormone. D. N. Henderson, Toronto.—p. 615.
Diagnosis and Treatment of Malignant Hypertension. C. P. Howard, Montreal.—p. 621.
*New Method of Treating Fractures in Distal Third of Femur. R. Anderson, Seattle.—p. 625.
Contribution to Study of Renal Anomalies. P. Bourgeois, Montreal.—p. 630.
Carcinoma of Small Intestine. F. D. Ackman, Montreal.—p. 634.
Infection of Mouth in Relation to Dysentery: Report of Case of Intestinal Amebiasis. P. Beregoff, Montreal.—p. 639.
The deRivas Thermal Method of Treatment in Intestinal Amebiasis. Pauline Beregoff, Montreal.—p. 641.
Nature of Postsplenectomy Anemia. R. Gottlieb, Montreal.—p. 642.
The Use of Hypnotics. V. E. Henderson, Toronto.—p. 645.
Radiation Therapy in Cancer of the Cervix. W. P. Healy, New York.—p. 647.
Bone Tumors and Irradiation. L. C. Kress and B. T. Simpson, Buffalo.—p. 651.
Latent Syphilis. S. C. Peterson, Winnipeg, Manit.—p. 655.
Clinical Survey of Twenty-One Cases of Intussusception. G. G. Miller and E. W. Workman, Montreal.—p. 660.
Hysterectomy. E. W. Mitchell, Toronto.—p. 665.
Tuberculosis in Childhood. D. A. Carmichael, Ottawa, Ont.—p. 670.

Treatment of Menorrhagia and Metrorrhagia by Anterior Pituitary-like Hormone.—Henderson treated thirty-nine cases of menorrhagia and metrorrhagia, presumably due to endocrine unbalance, with the anterior pituitary-like gonadotropic hormone from the urine of pregnancy; thirty-one patients were relieved of the menorrhagia and twenty-five had a complete return to normal menstruation. Of eight patients who failed to respond to treatment, four were proved to have local pelvic lesions sufficient to cause the complaint. Successful results from this form of therapy can be obtained only in the absence of pathologic lesions of the genital tract. Moderate diffuse enlargement of the uterus is frequently encountered in functional bleeding and is not a contraindication to hormone therapy. Harmful effects from the administration of anterior pituitary-like hormone are considered unlikely and are outweighed by the excellent therapeutic results. Improvement in the patient's general sense of well being after treatment is noted, and frequent relief of dizziness, when associated with menorrhagia, is observed. More exacting methods of diagnosis of pituitary and ovarian dysfunction are necessary before the full value of anterior pituitary-like hormone therapy will be realized.

Fractures in Distal Third of Femur.—Fractures of the distal third of the femur, under which category Anderson classifies the intercondylar and supracondylar forms, no longer prove

difficult to manage when one is employing a method of fracture treatment the chief principles of which are (1) a new and simple means of overcoming the deformity caused by the gastrocnemius and allied muscles and (2) the utilization of the well leg for countertraction. A working analysis of this mode of reducing supracondylar fractures includes correcting the posterior displacement of the distal fragment by wire or pin transfixion, which also acts as a traction agent; incorporating this transfixion in a plaster-of-paris cast to prevent recurrence of posterior deformity and to supply a means of immobilizing the fracture, and using an original splint, whereby only the well leg is required for countertraction. The author's technic differs in many respects from the prevailing manner of treating these fractures. Traction is not applied with the knee joint in flexion, as it is not necessary here to relax the gastrocnemius; on the contrary, by immediate anterior replacement and fixation of the distal third the lower extremity is held with the knee in full extension, thereby eliminating delay in completing reduction. Under the current mode these fractures call for the maximum of after-care, while this incorporated-pin method requires minimal attention. For this type of fracture it is obligatory to do more than to correct the shortening and to overcome the lateral displacement; it is necessary to overcome the posterior displacement of the distal fragment, besides correcting the plantar contraction of the foot. The steps of the procedure and the after-care are outlined.

Colorado Medicine, Denver

32: 433-512 (June) 1935

Endocrine Seminar: General Introduction. C. F. Kemper, Denver.—p. 444.
Structure of Endocrine Organs. H. M. Kingery, Denver.—p. 446.
More Important Pathologic Lesions Associated with Endocrinopathies. G. Z. Williams, Denver.—p. 448.
Brief Survey of Physiologic Function of Some of the Endocrine Glands. B. B. Longwell, Denver.—p. 454.
Clinical Syndromes. T. P. Sears, Denver.—p. 457.
Surgery of the Ductless Glands. G. E. Cheley, Denver.—p. 460.
Comments on Some Clinical Uses of Hormones. C. F. Kemper, Denver.—p. 463.
Changing Concepts in Treatment of Nephritis. H. Gauss, Denver.—p. 466.
Classification of Nephritis. W. C. Johnson, Denver.—p. 469.

Florida Medical Association Journal, Jacksonville

21: 537-580 (June) 1935

Peptic Ulcer from Medical Standpoint. W. C. Pumpelly, Fort Pierce.—p. 547.
Diabetes Treated by Radiation of Hypophysis. M. Dobrin and J. H. Lucinian, Miami.—p. 550.
Lung Abscess. F. G. Slaughter, Jacksonville.—p. 551.
Acute and Chronic Diseases: An Appreciation of Thomas Sydenham's Book. T. F. Hahn, DeLand.—p. 554.
The Black Widow Spider. F. T. Barker, Tampa.—p. 557.

Indiana State Medical Assn. Journal, Indianapolis

28: 267-312 (June 1) 1935

Ophthalmologic Aspect of Allergy. B. J. Larkin, Indianapolis.—p. 267.
*Malignancy Engrafted on Actinomycosis. F. M. Ruby, Union City.—p. 271.
Study of Modern Classification of Kidney Disease. S. W. Schneck, Mount Carmel, Ill.—p. 274.
Infant Diarrhea, with Especial Reference to Apple Therapy. C. A. Tompkins, Indianapolis.—p. 278.
Sources of Error in Radiography of Acute Mastoiditis. L. A. Smith, Indianapolis.—p. 280.
Report on Scarlet Fever Immunization. A. W. Cavins, Terre Haute.—p. 283.
The Management of Patients Exposed to Rabies. V. K. Harvey and C. G. Culbertson, Indianapolis.—p. 284.
The Prostate. A. J. Sparks, Fort Wayne.—p. 286.

Carcinoma Engrafted on Actinomycosis.—Ruby believes that carcinoma of the cheek, mouth and jaw is usually engrafted on a previous irritant condition. Syphilis is usually present, but its etiologic importance is not fully understood. Tobacco was used in just about the percentage of cases of cancer of the mouth as in all men regardless of a malignant condition. Roentgen treatment to be successful must be massive—that is, a single lethal dose seems to be best in a case in which the involvement also includes an irritant like the actinomycosis. The efficiency of radical surgery is doubtful, to add to the patient's comfort, even though it might somewhat prolong his life. A case is reported in which all the predisposing causes were present; but it was only after an attack of actinomycosis that the malignant condition was manifested. Leukoplakia was present, but so were the characteristic sulphur granules and the ray fungus. Also, as typical sinuses appeared below the mandible, the watery yellowish discharge contained the granules in amazing numbers. When after eight or nine months the case was reviewed, the actinomycosis had disappeared but the leukoplakia and the carcinoma were still present.

Journal of Experimental Medicine, New York

61: 735-874 (June 1) 1935

Studies on Bacterial Localization: Effects of Specific Immunization and of Gum Acacia Medium on Localization of Type I Pneumococci in Mice. L. Catron, Chicago.—p. 735.
Studies on Meningococcus Infection: VIII. Type I Specific Substance. H. W. Scherp and G. Rake, New York.—p. 753.
Cellular Reactions to Acetone-Soluble Fat from Mycobacteria and Streptococci: Effect of Neutralization on Biologic Activity of Tuberculolipoid and of Phthioic Acid Derived from It. K. C. Smithburn and Florence R. Sabin, New York.—p. 771.
Formation of Agglutinins Within Lymph Nodes. P. D. McMaster and S. S. Hudack, New York.—p. 783.
Rabbit Pox: III. Report of Epidemic, with Especial Reference to Epidemiologic Factors. H. S. N. Green, New York.—p. 807.
Multiplication in Vitro of Pseudorabies Virus in Testicle Tissue of Immunized Guinea-Pigs. E. Traub, Princeton, N. J.—p. 833.
Studies on Suprarenal Cortex: IV. Effect of Sodium Salts in Sustaining Suprarenalectomized Dog. G. A. Harrop, L. J. Soffer, W. M. Nicholson and Margaret Strauss, Baltimore.—p. 839.

Journal of Pharmacology & Exper. Therap., Baltimore

54: 1-136 (May) 1935

Mode of Action of Certain Drugs Which Stimulate Respiration. S. Wright, London, England.—p. 1.
Investigation of Toxicity and Hypoglycemic Effect of Several Guanidine Compounds. G. S. Samuelsen, Brooklyn.—p. 17.
Respiratory Effects of Morphine, Codeine and Related Substances: IV. Effect of α-Mono-Acetylmorphine, Mono-Acetyldihydromorphine, Diacetylmorphine (Heroin) and Diacetyldihydromorphine on Respiratory Activity of the Rabbit. C. I. Wright and F. A. Barbour, Ann Arbor, Mich.—p. 25.
*Use of Sodium Formaldehyde Sulphoxylate in Acute Mercury Poisoning. S. M. Rosenthal, Washington, D. C.—p. 34.
Ventricular Response in Caffeine Nicotine Antagonism. R. H. Cheney, Brooklyn.—p. 42.
Comparison of Motor Effects of Morphine, Codeine and Dihydromorphinone Hydrochloride (Dilaudid) on Thiry Fistulas. R. P. Walton and C. F. Lacey, New Orleans.—p. 53.
Absorption of Drugs Through the Oral Mucosa. R. P. Walton and C. F. Lacey, New Orleans.—p. 61.
Sodium N-Methyl-Cyclohexenyl-Methyl-Barbituric Acid (Evipal): Hypnosis, Anesthesia and Toxicity. A. H. Maloney and R. Hertz, Washington, D. C.—p. 77.
Remarks on Distribution of Barbiturates in the Brain. T. Koppanyi and J. M. Dille, Washington, D. C.—p. 84.
Studies of Phenanthrene Derivatives: IV. Veratrine-like Action on Skeletal Muscle of Certain 9-Substitution Products of Phenanthrene. R. G. Smith, Ann Arbor, Mich.—p. 87.
Identity of Reducing Substance in the Urine of Normal Persons Following the Ingestion of Amidopyrine. M. Enklewitz, New York.—p. 100.
True Methyl Cholines. A. Simonart, Louvain, Belgium.—p. 105.
Beta-Methylcholine Chloride and Its Acetyl Ester. R. T. Major and J. K. Cline, Rahway, N. J.—p. 131.

Use of Sodium Formaldehyde Sulphoxylate in Acute Mercury Poisoning.—Rosenthal outlines the use of formaldehyde sulphoxylate in acute mercury poisoning on a basis of its pharmacologic behavior. In its toxic action mercury produces cellular damage which, once sustained, will not be greatly benefited by this therapy. If sufficiently large doses of sulphoxylate are given by mouth it will pass throughout the alimentary canal and reduce any mercuric chloride to mercurous compounds, which are relatively harmless in the digestive tract. The oral administration of the antidote as early as possible is therefore of the greatest value because of the action on mercury and because of the local protection afforded the alimentary canal. Following intravenous injections of the drug, the blood serum will promptly reduce mercuric chloride to brownish black mercurous compounds. Intravenous therapy will prevent renal injury from mercuric chloride given subcutaneously. It will antagonize intravenous injections of mercuric chloride if injected before the mercury; treatment subsequent to intravenous injections of mercury is much less effective because of the promptness with which cellular injury is produced by this method of intoxication. The purpose of intravenous therapy is to protect the kidneys from any mercury in the tissues or alimentary tract

that is not promptly reached by the oral therapy. It is on this basis that the administration of sulphoxylate has been arranged so that effective amounts will be present in the body for from ten to twelve hours. No toxic effects from the treatment have been encountered in fifty human cases. A limitation of the dose and time of administration of the second injection of sulphoxylate has been suggested, however, in order to lessen such possibilities. The technic suggested for treatment of mercuric chloride poisoning in adults is: 1. Gastric lavage is done with a 5 per cent solution of sulphoxylate, about 200 cc. being left in the stomach. 2. Immediately following this, 10 Gm. of the drug is dissolved in from 100 to 200 cc. of distilled water, to be slowly injected intravenously, from twenty to thirty minutes being permitted for the injection. 3. In severe cases the intravenous injection is repeated from four to six hours following the completion of the first injection, from 5 to 10 Gm. being injected. 4. If colitis develops later, high colonic irrigations with a 1:1,000 solution of sulphoxylate is indicated.

Journal of Thoracic Surgery, St. Louis

4: 445-546 (June) 1935

Primary Malignant Tumors of Thymus Gland: Report of Two Cases. H. R. Decker, Pittsburgh.—p. 445.
Bronchiectasis: Study of One Hundred Proved Cases. E. Fletcher, London, England.—p. 460.
Multiple Intercostal Neurectomy for Pulmonary Tuberculosis: Indications and Results. J. W. Strieder and J. Alexander, Ann Arbor, Mich.—p. 473.
Chest Immobilization in Pulmonary Tuberculosis: Experimental Study. F. M. Foote and J. W. Spies, New Haven, Conn.—p. 492.
Thoracoplasty and Contralateral Artificial Pneumothorax. W. C. Pollock, Denver.—p. 502.
*Phrenic Exeresis in Conjunction with Artificial Pneumothorax Therapy. W. C. Pollock and J. H. Forsee, Denver.—p. 509.
Effect of Diaphragmatic Paralysis on Efficiency of Cough. J. Fine and A. Starr, Boston.—p. 525.
Secondary Aspergillosis (Aspergillus Niger) Superimposed on Bronchiectasis: Report of Case. G. D. Cannon, Waverly Hills, Ky.—p. 533.
Methods of Producing Experimental Pleural Conglutination. H. Landt, O. R. Hyndman and H. M. Korns, Iowa City.—p. 536.
Involvement of Sympathetic Nerves as a Complication of Acute Empyema. F. C. Hill, Omaha.—p. 539.

Phrenic Exeresis in Conjunction with Pneumothorax Therapy.—Pollock and Forsee believe that hemidiaphragmatic paralysis is of value as a supplement to artificial pneumothorax therapy when additional pulmonary compression and relaxation are required for cavity obliteration because of pleuropulmonary adhesions. Artificial pneumothorax complicated by acute pleuritis with or without serous effusion frequently ends in obliterative pneumothorax. Untimely obliteration of the pneumothorax space with pulmonary reexpansion will end in disease progression, and some procedure of compression therapy should be substituted for the pneumothorax lost through obliteration. The authors advocate that the next procedure instituted should be diaphragmatic paralysis. After successful pneumothorax, diaphragmatic paralysis is indicated as a preexpansion procedure. The elevation of the diaphragm decreases the size of the hemithorax and thus reduces the degree of pulmonary reexpansion required, prevents mediastinal retraction and causes a permanent continuation of some compression and relaxation. There is also the safety factor of decreased pulmonary function. Hemidiaphragmatic paralysis aids in compression and relaxation when pneumothorax is of an unsatisfactory character because of pleural symphysis over the involved lobe or lobes. This procedure may prevent recourse to radical surgical collapse. Hemidiaphragmatic paralysis is indicated when artificial pneumothorax, after a sufficient period, fails to obliterate midlung cavities, though no offending pleural adhesions are evident by roentgen examination. Diaphragmatic paralysis is of value when factors are present that tend to make artificial pneumothorax unsatisfactory and when, though the pneumothorax therapy has been successful, reexpansion of the compressed lung is contemplated. When factors are present that interfere with compression and relaxation of the treated lung, diaphragmatic paralysis has proved of value. If it is of value under unfavorable conditions, its value increases when favorable factors exist, and, since it is of value as a preexpansion procedure, the authors see no reason why practically all cases of artificial pneumothorax should not be supplemented by diaphragmatic paralysis.

Kentucky Medical Journal, Bowling Green

33: 253-298 (June) 1935

Practical Application of Our Present Knowledge of Tuberculosis, Particularly as It Applies to Children. L. C. Coleman, Richmond.—p. 255.
Whooping Cough. T. J. Marshall, Paducah.—p. 259.
Present Status of Whooping Cough. A. A. Shapero, Louisville.—p. 261.
Female Endocrinology. D. M. Cox, Louisville.—p. 265.
Unusual Foreign Body in Abdomen. D. P. Hall, Louisville.—p. 271.
Adenomatous Goiter. F. W. Rankin and A. E. Grimes, Lexington.—p. 273.
Treatment of Secondary Anemia with Liver Extract. W. Bloch, Louisville.—p. 276.
Giant Urticaria Due to Functional Dysmenorrhea. H. S. Frazier, Louisville.—p. 278.
Silicosis. O. O. Miller, Louisville.—p. 280.
Etiology and Surgical Treatment of Anal Fistula. W. J. Martin Jr., Louisville.—p. 287.
Subacute Bacterial Endocarditis: Case Report. J. P. Glenn, Russellville.—p. 295.

Medical Annals of District of Columbia, Washington

4: 119-152 (May) 1935

The Cause of Death. W. M. Yater and H. H. Hussey, Washington.—p. 119.
Treatment of Ocular Injuries. O. Wilkinson, Washington.—p. 124.
Fundamentals of Internal Medicine: Applied Pharmacodynamics: Rational Therapeutics. T. Koppanyi, Washington.—p. 127.
The Doctor and His Business Relations. F. A. Fenning.—p. 133.
Medical Economics: Coordination of Resources for Medical Care in the District of Columbia. W. M. Yater and R. Garrett, Washington.—p. 138.

New England Journal of Medicine, Boston

212: 1017-1068 (May 30) 1935

*Abnormal Bleeding in Women After the Age of Fifty. F. A. Pemberton, Boston, and J. S. Lockwood, Brookline, Mass.—p. 1017.
Development in Treatment of Pulmonary Tuberculosis from 1696 to the Present Time. G. M. Balboni, Boston.—p. 1020.
*Arthritis and Tonsillar Infection. H. A. Nissen, Boston.—p. 1027.
Obstetric Complications. J. M. Bergland, Baltimore.—p. 1033.
Recent Changes in German Health Insurance Under the Hitler Government. M. M. Davis and Gertrud Kroeger, Chicago.—p. 1037.
Study of Heart Disease Among Veterans: IV. Analysis of More Frequent Types of Anatomic Heart Disease. P. B. Matz, Washington, D. C.—p. 1042.

Abnormal Bleeding in Women After the Age of Fifty.—Pemberton and Lockwood investigated a consecutive series of 596 patients treated at the Free Hospital for Women with abnormal uterine bleeding as one of their complaints, 293 of whom were found to have benign lesions at the first operation. They conclude that, when the clinical evidence points toward the presence of carcinoma of the endometrium, a hysterectomy should be performed in spite of negative results by curettage, particularly when the patient is a nullipara who has passed the menopause. The treatment of elderly patients with uterine bleeding of any type is not complete without biopsy or thorough examination of the cervix to rule out carcinoma, even though there may be an obvious lesion elsewhere in the genital tract. About 50 per cent of women who report abnormal bleeding after the age of 50 will prove to have cancer as a cause. Some authorities have advocated doing a complete hysterectomy without curettage in any patient who bleeds after the menopause, on the ground that she almost certainly has cancer of the endometrium. In the present study there were twenty-seven patients with polyps who would have been operated on unnecessarily if an intra-uterine examination had not been done.

Arthritis and Tonsillar Infection.—To learn more about the association between tonsillar infection and joint disorders, Nissen studied nearly 500 arthritic patients. Even without recognized association between infections of the upper part of the respiratory tract and joint infection, such association may be present. Proof of this depends on intensive study of the individual to determine three factors: 1. Recognition of obvious and concealed chronic infection in the nasopharyngeal tissue. The two most common are unmistakable, the acutely infected tonsil and the red hypertrophied chronic tonsil. The third is possibly of greater importance and is often missed unless the patient is seen frequently, and the appearance, subsidence and reappearance of signs of infected lymphoid tissue are noted. On examination of this type of throat a purplish red discoloration is seen on the anterior tonsillar pillar, along the edges of the soft palate and at times in the uvula. These local changes are

constant to a certain degree (the dusky discoloration being present at all times) but show varying reactions to exogenous and endogenous infection. During such reactions the tonsillar poles become prominent and more inflamed, but this is noted only if the upper part of the tonsil is exposed. The duration of the reaction is short if the excitor is endogenous, long if of exogenous origin. 2. Recognition of joint and other systemic infection. This depends on thorough physical, laboratory and roentgen examinations. 3. Determination of association between local and joint and systemic infection by extensive and prolonged study of each individual patient.

Public Health Reports, Washington, D. C.

50: 725-764 (May 31) 1935

*Prevention of Intranasally Inoculated Poliomyelitis of Monkeys by Instillation of Alum into Nostrils. C. Armstrong and W. T. Harrison.—p. 725.
Tularemia: Susceptibility of the White-Tailed Prairie Dog, Cynomys Leucurus Merriam. G. E. Davis.—p. 731.
*Use of Below Freezing Temperatures for Maintenance of Meningococcus Cultures (Neisseria Intracellularis Weichselbaum). Anna M. Pabst.—p. 732.

Prevention of Intranasally Inoculated Poliomyelitis of Monkeys.—Armstrong and Harrison observed that the instillation of 4 per cent sodium aluminum sulphate into the nostrils of monkeys resulted in the survival of seventeen of a group of twenty-three animals, while only three of a group of nineteen nonprepared controls survived similar intranasal inoculation with poliomyelitis virus. Poliomyelitis tended to develop later and to run a slower course in the alum prepared group than in the nonprepared controls. The protective action of the alum solution is believed to be due to an alteration that decreases the permeability of the mucous membrane of the nose rather than to an antiseptic action.

Use of Below Freezing Temperatures for Maintenance of Meningococcus Cultures.—Pabst preserved ten chosen strains of meningococci in neutral glycerin at — 15 C. for two years with no apparent change in viability, morphology or serologic or biochemical characteristics. Two hundred and twenty-three strains have been stored at this temperature on dextrose agar slants, both with and without glycerin, with no appreciable loss of viability in the eight months during which they have been under observation.

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Surgery, Gynecology and Obstetrics, Chicago

60: 1033-1162 (June) 1935

*Hyperparathyroidism: Clinical Diagnosis and Operative Technic of Parathyroidectomy. F. H. Lahey and G. E. Haggart, Boston.—p. 1033.
Mechanism, Symptoms and Treatment of Hernia into Descending Mesocolon (Left Duodenal Hernia): Plea for Change in Nomenclature. C. L. Callander, G. Y. Rusk and Alma Nemir, San Francisco.—p. 1052.
Use of Vital Staining and Wet Films in Diagnosis of Lesions of Cervix. R. K. Bowes and N. R. Barrett, London, England.—p. 1072.
Studies on Peripheral Vascular Phenomena: IV. Finger Volume Changes in Patient Showing Raynaud's Phenomena. C. A. Johnson and R. N. Hedges, Chicago.—p. 1077.
*Electrosurgical Aseptic Intestinal Anastomosis. R. P. Wadhams and V. Carabba, New York.—p. 1082.
Activity of Hair Follicles with Reference to Pregnancy. Mildred Trotter, St. Louis.—p. 1092.
*Operation for Tuberculous Empyema. L. Eloesser, San Francisco.—p. 1096.
Birth Fractures of Femur. Å. Rydén, Lund, Sweden—p. 1098.
*Peripheral Nerve Block in Obliterative Vascular Disease of Lower Extremity: Further Experience with Alcohol Injection or Crushing of Sensory Nerves of Lower Leg. R. H. Smithwick and J. C. White, Boston.—p. 1106.
Uretero-Intestinal Implantation with Drainage by Extraperitoneal Catheter. F. Hinman, San Francisco.—p. 1115.
Anterior Gastro-Enterostomy by Short Loop Method. C. E. Rees, San Diego, Calif.—p. 1125.
Mesenteric Cysts: Brief Discussion and Report of Three Cases. C. S. Roller, Colusa, Calif.—p. 1128.
Teratoma of Spinal Cord. P. C. Bucy and D. N. Buchanan, Chicago.—p. 1137.

Hyperparathyroidism.—The diagnosis of hyperparathyroidism, Lahey and Haggart state, depends primarily on (1) an analysis of the chemical observations and (2) a survey of the roentgenograms of the bones of the skeleton and also of the kidneys. With the diagnosis of hyperparathyroidism established, the parathyroid adenoma should be found and removed. Failure to find parathyroid adenomas in many cases will be due to failure to realize the frequent atypical location of the parathyroids and failure to investigate the possible atypical locations for a possible parathyroid adenoma. With the prethyroid muscles severed, the middle thyroid veins are ligated between clamps so that the lateral vascular attachments of the thyroid to the internal jugular vein are severed. The outer border of the thyroid is then grasped with forceps and rotated inward. The internal jugular vein and common carotid artery are completely separated from the back of the thyroid and the inferior thyroid artery completely demonstrated as a trunk where it passes behind the common carotid artery. The back of the gland is inspected, and if a tumor cannot be seen the gland is palpated for such a tumor within the gland. An adenoma of a parathyroid usually converts that structure into a globular mass and changes its color to a pale white rather than the brownish color characterizing the typical normal parathyroid. Should no parathyroid adenoma be demonstrable on this exposure, the inferior thyroid artery must be completely dissected up to its entrance into the thyroid gland. The recurrent laryngeal nerve must be found and dissected up to its passage behind or in front of the inferior thyroid artery. If still no parathyroid adenoma is found, one must expose the groove between the trachea and the esophagus in the region of the inferior thyroid artery. If still the adenoma is undemonstrated, the superior thyroid artery should be ligated and the upper pole of the thyroid turned downward, so that the region where it rests against the thyroid cartilage may be inspected. At this point caution must be exercised, as the recurrent laryngeal nerve enters the larynx here, at the point where the lowest fibers of the inferior construction are inserted into the horn of the thyroid cartilage. If the tumor is still not found, the thyroid should be palpated through and through between the thumb and the forefinger and any discrete globular nodule within the gland exposed by an incision into the gland, removed and submitted to the pathologist for immediate frozen section report. If failure to demonstrate the parathyroid tumor persists, the search is continued in the bundles of the superior thyroid vessels, out along the main trunk of the inferior thyroid artery, behind the esophagus and along the inner aspect of the upper pole. The isthmus is palpated against the trachea. If a pyramidal lobe is present it is exposed and palpated throughout its extent. If the evidence of the existence of hyperthyroidism is certain and still no parathyroid tumor has been found, and if digital palpation of the superior mediastinum demonstrates no palpable parathyroid tumor, the manubrium of the sternum may be removed to facilitate a visual search for a mediastinal parathyroid adenoma. Should exposure of all these regions fail to demonstrate an adenoma of a parathyroid, it then becomes justifiable to remove and submit a normal appearing parathyroid to the pathologist for decision as to the possible presence of hyperplasia of the parathyroids.

Electrosurgical Aseptic Intestinal Anastomosis.—Wadhams and Carabba do not agree with Ward that the electrocoagulation procedure for intestinal anastomosis cannot be relied on for the stomach with its redundant mucosa. The failure is one of lack of properly performing the electrosurgical technic, especially as to the depth and strength of the current and the degree of coagulation. In the authors' experience the technic of Briggs and Whitaker, calling for only one row of sutures, is adequate. In retrospect there are only extremely rare instances in which immediate anastomoses are necessary. In cases in which immediate intestinal drainage is necessary, temporary ileostomy, colostomy or appendicostomy may be performed. In cases of intestinal resection, the anastomosis can be performed below the lumen of the resected intestine and the lumen allowed to drain externally while the anastomosis forms and begins to function. The authors have not had a case of secondary hemorrhage in fifteen consecutive operations by their method, which they describe. All the animals were carefully watched after operation and at necropsy for this complication. They believe that the possible applications of the technic to the human being are: 1. Gastro-enterostomy—by electrocoagulation, when such a procedure is necessary in repairing a per-

forated duodenal ulcer complicated by stricture. 2. Lateral anastomosis after resection of segments of the intestine secondary to partial gangrene of a portion of the intestine, as in strangulated Richter's hernia, gangrene due to bands, or femoral hernia. The two open ends of the loop are left externally for drainage until the obstruction is relieved. The fistula can be then allowed to close spontaneously or repaired secondarily. This procedure can be applied in performing an enterocolostomy. 3. Ileosigmoidostomy as a preliminary procedure to resection of the cecum and ileosigmoidostomy of choice with a temporary colostomy or appendicostomy. 4. Completion of the Mikulicz operation in the first stage of the operation, with elimination of the secondary clamping. 5. Cholecystogastrostomy or enterostomy. 6. Anastomosis of the ureters to the large intestine. 7. Without obstruction, primary resection of the large intestine with side-to-side anastomosis, instead of the Mikulicz operation. The authors performed fifteen consecutive and diversified anastomoses on the dog and one on man successfully by the electrocoagulation technic without mortality, leakage, infection or hemorrhage.

Operation for Tuberculous Empyema.—Eloesser's desire to obviate a drainage tube led to an operation that has proved of use in a number of secondarily infected tuberculous empyemas. It has been used in a few obstinately toxic tuberculous empyemas in which no pus forming organisms could be found. The operation causes the underlying lung to expand; it is therefore not applicable to empyemas in which the lung is so badly affected that expansion to any degree seems inadvisable. The question of applicability must be decided by clinical pulmonary symptoms and especially by roentgenograms taken prior to the appearance of the complicating empyema. Under local anesthesia a U-shaped flap of skin and subcutis is outlined about half way between the posterior axillary line and the line of the inferior scapular angle. The flap has a base about 2 inches wide, which lies about one rib higher than the bottom of the empyema cavity, so that the rising diaphragm may not stop drainage; it is about 2½ inches long, the length of two ribs and their intercostal spaces, long enough to reach into the pleural cavity without the least tension. The rib underlying the top of the flap is resected, the amount resected equaling the width of the flap. If the flap is too narrow and the resection too scant, drainage will be insufficient. The rib should be stripped with a cautery instead of a raspatory and the bared intercostal nerve injected with 1 cc. of absolute alcohol. The tip of this flap is turned into the chest and tacked to the pleura with one or two chromic catgut stitches; the edges of the defect in the skin are approximated with a few stitches of silkworm. This thoracotomy needs no tube, for the skin flap which lies against the soft parts of the chest keeps the wound open. It remains open until the lung reaches the chest wall, after which it spontaneously and automatically closes. It has a valve action; each cough or rise in intrapulmonary air pressure expels a little air from the thorax and causes a gradually increasing negative pressure in the empyema cavity. It is more difficult for air to enter through this valvelike wound than to escape from it. Dressings should be left in place as long as possible —for many days.

Peripheral Nerve Block in Obliterative Vascular Disease.—Smithwick and White point out that peripheral nerve block is an effective method of controlling rest pain in patients with advanced obliterative vascular disease. Besides controlling pain, the circulation to the part may be increased because the anesthetic area is also deprived of its vasoconstrictor nerves. Local infection in open lesions is more easily controlled because frequent antiseptic dressings can be done painlessly. The general condition of the patient improves with the relief of pain, and other conservative measures become more effective. The operation requires careful technic and asepsis and should be done in multiple stages. The nerves may be either injected with alcohol or crushed. The latter method is more simple and equally effective, although the nerves regenerate more rapidly. The authors believe that this procedure has more than halved the number of necessary major amputations and more than doubled the number of successful minor amputations. It also has increased the number of cases in which no amputation is necessary. They emphasize the striking reduction in bilateral major amputations in their forty-five cases. The results are better in the patients with thrombo-angiitis obliterans than in the arteriosclerotic group. Patients with pulsation of the popliteal vessels do better than those in whom the vessel is obliterated at this level. Amputation of uninvolved toes is an effective prophylactic procedure in selected cases. If the vasomotor index is high, lumbar ganglionectomy should be done after the peripheral nerves have regenerated in certain cases. Unless hopeless gangrene or infection sufficient to endanger the life of the patient is present, this operation should be tried before a major amputation is resorted to. It is not indicated in the early treatment of obliterative vascular disease but should be used in advanced stages after other conservative methods have proved inadequate.

Virginia Medical Monthly, Richmond

62: 123-184 (June) 1935

Parathyroid Glands in Health and Disease. W. Bauer, Boston.—p. 123.
Vomiting in the New-Born, with Especial Reference to Duodenal Atresia: Report of Two Cases. T. D. Walker Jr., W. W. Falkener, Newport News, and J. S. Horsley, Richmond.—p. 141.
The Irritable Colon: Common Condition, Commonly Misunderstood. T. D. Davis, Richmond.—p. 144.
Strips of Fascia Lata as Suture Material in Repair of More Difficult Abdominal Hernias. J. C. Masson, Rochester, Minn.—p. 148.
*Leiomyoma of Gastro-Intestinal Tract: Report of Two Cases. R. D. Jones Jr., Norfolk.—p. 150.
Prosthetic Obturator and Plumper. J. B. Williams, Richmond.—p. 155.
Siamese Twins at Full Term: Report of Case. E. L. Johnson, Bedford. —p. 157.
Review of Papers Read at Meeting of the American Society of Clinical Pathologists. Regena Cook Beck, Richmond.—p. 158.
Some Observations on Care and Treatment of Diseased Tonsils. B. Lee, Pulaski.—p. 162.
Chemical Injury of Cornea in the New-Born: Report of Experiments. S. Trattner, Richmond.—p. 163.

Leiomyoma of Gastro-Intestinal Tract.—Jones presents two cases of leiomyoma of the gastro-intestinal tract observed during the last two years. He states that gastro-intestinal leiomyomas may be intraluminary or extraluminary, depending chiefly on the layer of muscle from which they are derived. For example, a tumor arising from the muscularis mucosa would more than likely be intraluminary and pedunculated, whereas one springing from the external layer would develop between the layers of the mesentery or, if opposite the mesenteric attachment, would by stretching the peritoneum become subserous. Many leiomyomas of the gastro-intestinal tract remain dormant and never produce symptoms worthy of note. On the other hand, they are capable of a wide variety of complications, depending on the location and size of the growth as well as the degree of malignancy. Submucous growths, for instance, are particularly prone to ulceration and hemorrhage. Such tumors may be the cause of gastro-intestinal bleeding of obscure origin. Ulceration may result in perforation and peritonitis. In the stomach, a submucous pedunculated growth may produce an intermittent pyloric obstruction, and in the small and large intestine it is not uncommonly the cause of intussusception. Subserous growths are rarely pedunculated, and Wolfer states that they may vary in size from that of a cherry to that of a mass filling the entire abdomen. Adhesions often develop, as the result of which the tumor may become fixed to the viscera or to the abdominal wall, thereby increasing the possibility of intestinal obstruction. In the case of the small intestine, angulation may be produced by the weight of the tumor, even in the absence of adhesions. When the growth is of the mixed type and encroaches on the mucosa, ulceration and hemorrhage may result, as it does in the intraluminary type. Leiomyoma should be considered in any case presenting vague abdominal symptoms, when a history of intermittent attacks of intestinal obstruction is obtained or when the case is complicated by gastro-intestinal hemorrhage of obscure origin. More often than not the tumor is not palpable, in which case the roentgenogram is of great value in the diagnosis. The treatment is surgical, the technical procedure depending on the immediate complications to be dealt with, the location of the growth, whether or not it is malignant, and in benign cases the risk of the operation versus the risk of carrying the tumor.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Dermatology and Syphilis, London

47: 181-222 (May) 1935

*Fractional Gastric Analysis in Diseases of the Skin: Further Observation in Three Hundred and Sixteen Cases, with Especial Reference to Rosacea. W. H. Brown, Mary S. Smith and A. D. McLachlan.—p. 181.

Case of Riehl's Melanosis: Notes on Classification of Poikilodermias. J. Kinnear.—p. 191.

Recurrent Menstrual Purpura and Vicarious Menstruation. P. Ellman and F. P. Weber.—p. 197.

Effect of Angle of Incidence on Dose of X-Rays Absorbed by Skin: Note. J. Kinnear.—p. 202.

Fractional Gastric Analysis in Diseases of the Skin.—Brown and his associates performed gastric analyses in 150 cases of rosacea, and compared the results with those of a previous investigation of fifty cases. For comparison, gastric analyses have been performed also in 166 cases of dermatoses other than rosacea. The percentage of cases showing achlorhydria and extreme hypochlorhydria is lower in the rosacea group, viz., 28 per cent, as compared with 35 per cent in other dermatoses. Symptoms of gastric disturbance were present in 61 per cent of a group of seventy-five patients with rosacea. The severity of the symptoms varied considerably in degree. In some they were negligible and in others they amounted to actual pain. The most common complaint was a sensation of fulness after food, with flushing of the face. The degree of flushing also varied greatly. A much more extensive study of the gastric analysis has led to the conclusion that marked subacidity is not a feature peculiar to rosacea as was originally thought. A degree of subacidity seems to be a feature of chronic dermatoses in general. The observations do not detract from the well established fact that strict dietetic treatment in combination with large doses of dilute hydrochloric acid brings about marked improvement in rosacea. A subacidity is frequent in rosacea and in other chronic dermatoses. It frequently follows the infectious fevers. In pernicious anemia and subacute combined sclerosis, achlorhydria is the rule. It is a feature also of the type of anemia described variously as microcytic, nonmegalocytic or simple achlorhydric anemia, and of the condition known as gastrogenic diarrhea and of certain glossitic and ulcerative disorders of the mouth. According to Ryle, the gastric habitus of the individual is closely related to the physiologic habitus. The one possible explanation of the subacidity found in chronic dermatoses is that the pain, discomfort or itching of a chronic dermatosis in time would tend to produce a depressed, debilitated, hypotonic individual. In the allergic complaints of the authors' series (Besnier's prurigo), in which one would expect the hypotonicity and the hypoacidity to be most marked owing to the long duration and distressing nature of the complaint, the subacidity was least marked of all the dermatoses. The rosacea patient, according to Rulison, is typically a person with poor muscle tone and a low blood pressure. It is likely that some degree of gastritis is always present in view of the dietary indiscretions indulged in by the patient. Although the duration and the severity of the disease in rosacea appear to bear but little relation to the gastric hydrochloric acid content, this may be explained by the constitutional factor. In a hypersthenic individual with hyperchlorhydria the presence of chronic gastritis may lead to reduction of the gastric acidity without bringing it below the level of hyperchlorhydria.

British Medical Journal, London

1: 1061-1108 (May 25) 1935

Acute Tonsillitis: Account of Some Recent Streptococcic Infections. F. E. Camps.—p. 1061.

*Tonsillitis and Albuminuria. O. L. V. S. de Wesselow, H. K. Goadby and D. C. L. Derry.—p. 1065.

Spirochetal Jaundice in a London Sewer Worker Confirmed by Laboratory Examinations. E. A. M. Halsted.—p. 1067.

Septicemia Due to Brucella Abortus Following Operation. L. S. Potter and N. Harburn.—p. 1068.

Weight Bearing Instruments for Walking. H. C. Trumble.—p. 1070.

Tonsillitis and Albuminuria.—In 354 cases of tonsillitis de Wesselow and his associates found 14.4 per cent that showed definite early albuminuria and 6.2 per cent late albuminuria. From the urinary and clinical observations it would seem probable that focal nephritis occurred in thirty-five (10 per cent) and diffuse glomerulonephritis in at least three (0.8 per cent). No correlation was found between the predominance of hemolytic streptococci in the throat at the time of the acute infection and the incidence of focal nephritis. Seasonal variations of external temperature did not appreciably affect the incidence of early or late albuminuria. The incidence of predominant hemolytic streptococcus infection in the throat was not greater in those patients who afterward complained of rheumatic pains than in the general series.

East African Medical Journal, Nairobi

12: 35-66 (May) 1935

Quinine as Prophylactic in Malaria. H. L. Duke.—p. 38.

Some Notes on Treatment of Fractures. C. V. Braimbridge.—p. 42.

Control of Bedbugs (Cimex Rotundatus): Notes. J. I. Roberts and D. A. Dick.—p. 46.

Poisoning by Jatropha Multifida, L.: Note on Cases. W. D. Raymond.—p. 57.

Glasgow Medical Journal

5: 249-328 (May) 1935

The Parathyroid Glands: Review of Anatomy, Physiology and Pathology of Parathyroid Glands, with Observations on Three New Cases of Generalized Osteitis Fibrosa Cystica. D. P. Cuthbertson and W. A. Mackey.—p. 249.

Carbohydrates in Treatment of Diabetes Mellitus. J. N. Cruickshank.—p. 293.

Journal of Pathology and Bacteriology, Edinburgh

40: 425-644 (May) 1935

Combined Treatment of Experimental Trypanosome Infections by Chemotherapeutic Agents. C. H. Browning and R. Gulbransen.—p. 425.

Tuberculous Arteritis. W. G. Barnard.—p. 433.

Mechanizing the Viable Count. J. A. Reyniers.—p. 437.

Staphylococcic Bacteriophages. F. M. Burnet and Dora Lush.—p. 455.

Psittacosis in the Developing Egg. F. M. Burnet and Phyllis M. Rountree.—p. 471.

Histologic Changes in Kidneys of Adrenalectomized Rats. S. L. Simpson and V. Korenchevsky.—p. 483.

*Tuberculous Meningitis in Children. J. W. S. Blacklock and Mary A. Griffin.—p. 489.

Hematologic Standards of Healthy Persons. C. Price-Jones, Janet M. Vaughan and Helen M. Goddard.—p. 503.

Immature Rabbit as an Experimental Urinary and Fecal Typhoid Carrier: Effect of Hexamine Treatment. M. Coplans.—p. 521.

Relationship of Eosinophil Leukocyte to Allergy and Anaphylaxis. A. C. P. Campbell, A. M. Drennan and T. Rettie.—p. 537.

Experimental Inhibition of Tumor Induction by Mustard Gas and Other Compounds. I. Berenblum.—p. 549.

Simple Superficial Esophageal Cast. T. C. Patterson.—p. 559.

*Rôle Played by Natural Antisheep Hemolysin and Effect of Heat on Reactivity of Serum in Wassermann Reaction. R. W. Fairbrother and A. L. P. Peeney.—p. 571.

New Culture Mediums Based on Sodium Desoxycholate for Isolation of Intestinal Pathogens and for Enumeration of Colon Bacilli in Milk and Water. E. Leifson.—p. 581.

Adenolymphoma of Salivary Glands. R. Carmichael, T. B. Davie and M. J. Stewart.—p. 601.

Tuberculous Meningitis in Children.—Blacklock and Griffin say that tuberculous meningitis is the most frequent form of meningitis in childhood. The primary site of infection in a series of 241 cases of tuberculous meningitis under 13 years was most frequently thoracic (73.9 per cent), then abdominal (22.8 per cent), of the cervical glands (2.1 per cent) and unknown (1.2 per cent). There was little difference in the sex distribution. Of the patients, 85.5 per cent were less than 6 years of age. The seasonal incidence was highest in the late spring and early summer months. The frequent association of tuberculous meningitis and generalized miliary tuberculosis is discussed; either lesion alone is uncommon. Human strains were easier to isolate directly by culture than bovine. In one case, in which infection with a human strain had occurred, the inoculated guinea-pig gave a negative result whereas the cultures were positive. From a clinical series of cases of cerebral tuberculosis seventy-two strains were isolated, of which 18.1 per cent were bovine, and from the primary lesions in a necropsy series 114 strains were obtained, of which 24.6 per cent were bovine. The highest percentage of bovine strains occurred in the third year of life in both series. The total bovine percentage obtained for meningitis from both series was 22.5 per cent and for all forms of cerebral tuberculosis 22 per cent. A higher percentage of bovine infections was noted in

country than in city children. Meningitis following primary thoracic lesions was nearly always due to the human type of bacillus, and that following primary abdominal lesions was usually due to the bovine type. Bovine strains were isolated in three cases of meningitis in which primary lung lesions were verified at necropsy. A case is described in which tubercle bacilli were isolated during life from the cerebrospinal fluid and in which tuberculomas were found at necropsy, but no meningitis.

Effect of Heat on Reactivity of Serum in Wassermann Reaction.—Irregular results appear not infrequently in the Wassermann reaction when a 1 : 2 dilution of serum is employed. Fairbrother and Peeney suggest the correction of the defect by inactivation at 58 C. An explanation of this phenomenon does not readily present itself. There appears to be no doubt that with the serum dilution of 1 : 2 complement is not completely fixed by the combination of the antigen and the reacting substance in the serum. It has been suggested that the natural antisheep hemolysin is the main responsible factor. If this were so it would indicate fixation of the complement during the initial incubation by the hemolysin alone rather than by the antigen-serum combination. The results show in an unequivocal manner that, when a satisfactory antigen is employed, any part played by the natural hemolysin is relatively insignificant. Correction of the irregularity was frequently obtained, irrespective of the presence of natural hemolysin, by means of further inactivation of the serum at 58 C. A second heating at 56 C. did not have this effect; therefore some important change had resulted from inactivation at the higher temperature. A further demonstration of this change was that the serums alone usually absorbed less complement. These results suggest that by inactivation at 58 C. some alteration, probably of a physicochemical nature, occurs in the serum and that the subsequent fixation of complement by the antigen-serum combination becomes greatly facilitated. In the routine test, owing to some peculiarity of individual serums, complete fixation of complement by the greatest concentration of the serum in the presence of antigen is prevented. The actual nature of this peculiarity, however, except that it is corrected by inactivation at 58 C., is unknown.

Journal of State Medicine, London

43: 311-372 (June) 1935

Rheumatism: Its Causes and Prevention. F. D. Howitt.—p. 313.
The Modern Science and Practice of Nutrition. A. P. Cawadias.—p. 323.
The Mantoux Tuberculosis Test in Children. A. M. Critchley.—p. 335.
Medical Services in a Village Settlement. L. B. Stott.—p. 339.
Early Diagnosis of Tuberculosis in Infancy and Childhood. B. Morgan.—p. 343.
Dental Lesions as First Sign of Disturbance of Physiologic Function. F. W. Broderick.—p. 352.
Great Epidemics of Middle Ages, with Especial Reference to Norwich and Norfolk. M. R. Taylor.—p. 361.
Spectrum Analysis as Aid in Medicine. H. Ramage.—p. 370.

Lancet, London

1: 1139-1198 (May 18) 1935

Vision and Its Disturbances in Relation to Cerebral Lesions. W. Harris.—p. 1139.
*Etiology of Acute Rheumatism: Experimental Evidence of Virus as Causal Agent. B. Schlesinger, A. G. Signy and C. R. Amies, note on photomicrographs by J. E. Barnard.—p. 1145.
*Relationship Between Adenomas and Cancer of Large Bowel. J. P. Lockhart-Mummery.—p. 1149.
Measuring Red Blood Cells, with Especial Reference to New Diffraction Apparatus. A. Pijper.—p. 1152.

Etiology of Acute Rheumatism.—According to Signy and his co-workers, the deposits obtained by high speed centrifugation of pericardial fluid in cases of acute rheumatic pericarditis contain particles that morphologically resemble virus elementary bodies. Similar bodies have been found in the deposit obtained from one pleural exudate in association with rheumatic pneumonia. Relatively pure suspensions of these bodies in formol saline solution have been prepared. These suspensions are specifically agglutinated by the serums of patients who are suffering from, and successfully resisting, an acute rheumatic infection. The serums of patients in whom the infection is quiescent fail, as a rule, to agglutinate these suspensions. Completely negative reactions were also obtained with the serum of normal persons and of patients suffering from various nonrheumatic infections. It is believed that the bodies found in pericardial exudates represent the actual infective agent of acute rheumatism. The importance of streptococcic infection as a factor in the etiology of the disease is recognized. It is suggested that the lowered resistance produced by such infections enables the virus to enter the body or, if the virus is already lying latent in the tissues, allows it to assume active characters. The characteristic properties of the infective agent of rheumatism cannot be closely paralleled with those of any known virus. Some of its characters, however, are shared by a number of virus agents.

Relation Between Adenomas and Cancer of Intestine.—In his follow up study of fifty operative cases of what was believed to be simple adenoma, Lockhart-Mummery observed that adenomas of the rectum or colon are not innocent growths and that they are merely a stage in the development of malignant tumors and should be so treated. At a certain age, some cells of the intestinal epithelium exhibit a tendency to undergo hyperplasia. This tendency is not confined to one cell or group of cells but appears to be fairly widespread, with the result that the removal of one adenoma does not prevent the development of others. The author believes that what happens, when a tumor forms, is that a change or gene mutation occurs to start with in the nucleus of a single cell, resulting in an excessive rate of reproduction of that cell as compared with the reproduction of normal cells of the same tissue. The adenoma results from the excessive reproduction of this single cell. The tumor is composed of normal cells differing, as far as can be observed, from other cells only in the fact that its cells are reproducing themselves too fast. This tendency for a mutation or change of their character to take place is often, however, present in a number of different cells in a fairly wide area. The exciting cause of the change may be due to genetic instability or to some factor in the environment, and the fact that it has occurred in one cell does not prevent the same change from taking place later on in other cells. From a practical point of view, local removal of the tumor would appear to be sufficient if the patient is observed at intervals of every four months during the next five to ten years, so that fresh tumors can be removed at once before they have had an opportunity of becoming malignant. But, unless the patient is kept under observation in this way, the development of other tumors is very likely to occur unobserved. The frequency of such a happening appears to be about 50 per cent, and a considerable danger exists of a malignant condition supervening.

Medical Journal of Australia, Sydney

1: 573-606 (May 11) 1935

Syme and Medical Education. B. T. Zwar.—p. 573.
Comments on Postoperative Pneumonia. K. W. Starr.—p. 579.
Hodgkin's Disease: Some Clinical Aspects, with Especial Reference to Effects on Hematopoietic Tissues and Nervous System. E. L. Cooper.—p. 585.

Quarterly Journal of Medicine, Oxford

4: 1-92 (Jan.) 1935

Some Observations on Etiology and Effect of Alkalis on Nephrotic Syndrome. R. B. Hawes and E. C. Vardy.—p. 1.
*Comparison of Pituitary Basophilic Syndrome and Adrenal Corticogenital Syndrome. F. G. Lescher, with report on pathology by A. H. T. Robb-Smith.—p. 23.
*Schüller-Christian Syndrome: Lipoid Granulomatosis with Defects in Bones, Exophthalmos and Diabetes Insipidus. F. L. Horsfall Jr. and W. R. Smith.—p. 37.
*Secretion of Urine in Diabetic Coma. R. A. McCance and R. D. Lawrence.—p. 53.
Primary Lymphogranuloma of Stomach: Report of Four New Cases. T. Thompson and L. H. Howells.—p. 81.

Pituitary Basophilic Syndrome and Adrenal Corticogenital Syndrome.—Lescher reports a case of carcinoma of the adrenal cortex, which shows all the cardinal and most of the occasional symptoms recently ascribed by Cushing to an adenoma of the basophil cells of the anterior lobe of the pituitary. Examination of serial sections of the pituitary gland showed some general increase in the basophil and acidophil cells, and at one point there was a small collection of the basophil cells, 0.3 mm. in diameter. In view of the case reported and

others of a somewhat similar kind from the literature, the author concludes that Cushing's syndrome, complete in its entirety, may be caused by such diseases as tumors of the adrenal cortex, and so a clinical distinction cannot always be made between these two syndromes. Every case of Cushing's syndrome should be critically examined, including a roentgen examination of the abdomen for a shadow in the renal areas and for the position of the kidneys. While it is generally accepted that the anterior lobe of the pituitary elaborates one or more gonadotropic secretions, there is no reliable evidence to show that the basophil cells are responsible for this. What evidence there is is rather against this theory. From the study of the basophilic syndrome and from observations that an excess of basophilic cells occurs in such diseases as hypertension, vascular sclerosis and chronic nephritis, as well as in old age, it may be that the basophil cells are a source of some depressive inhibitory substance that can produce such conditions as a low metabolic rate, altered carbohydrate metabolism, obesity, lethargy and lack of sex functions.

Schüller-Christian Syndrome. — Horsfall and Smith observed a case of the Schüller-Christian syndrome during two admissions to the hospital, and finally they performed a complete necropsy. Pathologic studies of the tissues indicate that the lesions are granulomatous in nature and contain large quantities of lipoids. Fractional chemical analyses of the lipoids in the lesions demonstrate the predominance of cholesterol. This confirms the work of other investigators. Fifty-nine other cases of Schüller-Christian syndrome have been collected from the literature. Thirty-six completely reported cases have been analyzed, and the disease is discussed on this basis. Although lipoid granulomatosis, as used by Chester, is more accurate than the term xanthomatosis, it is suggested that the former could with more exactness be modified to cholesterol granulomatosis.

Secretion of Urine in Diabetic Coma.—McCance and Lawrence state that diabetic coma may be accompanied or followed by a disorganization of renal function characterized by (1) an oliguria, which is not invariable and often transitory, (2) a retention of urea, creatinine (and probably uric acid), which may outlast the oliguria by some days, (3) a retention of ketone bodies (if present), (4) a retention of sugar (if present above threshold limits), (5) a very acid urine (P_H usually about 5), (6) a normal excretion of ammonia, (7) no loss of the acid base regulating mechanisms associated with salt excretion, (8) no constant anatomic lesion and (9) a tendency to recovery with absence of sequels. A similar and possibly identical syndrome has been encountered in two noncomatose diabetic patients and may be relatively common and be closely allied to the renal dysfunctions of intestinal intoxication and Addison's disease. The real cause is unknown. There is no specific treatment. If the patient lives, insulin and fluids (especially perhaps salines) will in time restore the function of the kidney.

Journal of Oriental Medicine, Dairen, South Manchuria

22: 65-80 (May) 1935

Early Tissue Reactions in Lungs of Rabbits After Intravenous Injections of Acid-Fast Bacilli: Part I. Examinations with Human Tubercle Bacilli. Y. Hisamochi.—p. 65.
Id.: Part II. Experiments with Bovine Tubercle Bacilli. Y. Hisamochi.—p. 66.
Id.: Part III. Experiments with Avian Tubercle Bacilli. Y. Hisamochi.—p. 67.
Id.: Part IV. Experiments with B C G Bacilli. Y. Hisamochi.—p. 68.
Id.: Part V. Experiments with Dr. Ota's So-Called Acid-Fast Bacilli of Human Lepra. Y. Hisamochi.—p. 69.
Id.: Part VI. Experiments with Timothee Bacilli. Y. Hisamochi.—p. 70.
Id.: Part VII. Experiments with Indian Ink. Y. Hisamochi.—p. 71.
Statistics on Opium Addicts in Mukden. Wang Shih-Kong.—p. 73.
Special Kidney Bleeding. K. Yajima.—p. 74.
Determination of "Comfort Zone" for Japanese and Manchurians: Part I. "Comfort Zone" for Train Passengers in Manchuria in Winter. H. Takabuchi.—p. 75.
Anencephalus Delivery: Three Cases. K. Saito.—p. 76.
Statistical Observation on Labor in the Dairen Hospital. S. Hara and M. Sasaki.—p. 77.
Cholera and Cholera-like Vibrio: Part IV. and V. Variability of Cholera Vibrio. K. Manako.—p. 79.

Presse Médicale, Paris

43: 857-872 (May 29) 1935

*Polycoric Hepatomegaly. R. Debré and G. Sémelaigne.—p. 857.
Extension Plaster Casts. G. Rieunau.—p. 861.
Meaning of Allergy. M. Jaquerod.—p. 862.

Polycoric Hepatomegaly.—In a previous article (*Presse méd.* **43:**801 [May 18] 1935) Debré coined the word polycoria. It is derived from the Greek and means pathologic accumulation of reserve substances in an organ resulting in its hypertrophy. In the present article Debré and Sémelaigne discuss various aspects of polycoric hepatomegaly. The clinical onset is gradual, usually occurring in the first months of life. The first sign observed is increased volume of the abdomen due to enlargement of the liver. In the majority there is no other sign. The enlargement is considerable, the liver occupying at least a third of the abdominal cavity and pressing the intestine down and to the left. There is never a collateral circulation or signs of portal hypertension or ascites. Disorders of growth are present, but their intensity is variable. Biochemical studies show metabolic disturbances affecting the carbohydrates and fats. There is usually a hypoglycemia in the morning. After ingestion of dextrose, the increased glycemia is slight and slow and the return to normal is equally slow and follows a prolonged phase of hypoglycemia. In three of their four patients the lipemia was markedly high. The evolution of the disease is distinctly chronic and spreads over several years. It must be differentiated from the familial hepatosplenomegalies and the disorders of lipoid metabolism. The pathologic anatomy is not yet completely known, but it may be stated that the characteristics are an enormous, smooth, pale liver of homogeneous appearance. The consistency and color on section are those of a liver affected with fatty degeneration. Microscopically, a massive accumulation of glycogen in the form of droplets in the cellular protoplasm is seen. The pathogenesis is uncertain, but the authors feel that the condition is a result of a neuroendocrine disorder affecting the glands which control carbohydrate metabolism, especially the system antagonistic to the pancreas-adrenals.

Schweizerische medizinische Wochenschrift, Basel

65: 509-548 (June 8) 1935. Partial Index

Transmission to Monkeys by Cutaneous Vaccination of Poliomyelitis and of Postvaccinal Encephalitis Occurring in the Netherlands. H. Aldershoff.—p. 510.
Bilateral Primary Cancer of Uterine Tubes. H. Beitzke.—p. 513.
Increase in Sheep's Blood Agglutinins in Glandular Fever and Diagnostic Value of Hetero-Agglutination. E. Glanzmann and F. Ottensooser.—p. 520.
*Dangers from Modern Industrial Poisons: Polyneuritis with Retrobulbar Neuritis After Working with Trichlorethylene. R. Isenschmid and E. Kunz.—p. 530.
*Cause of Jaundice in Spirochaetosis Icterohaemorrhagica Inada (Weil's Disease). R. Kaneko.—p. 531.

Industrial Poisons as Cause of Neuritis. — Isenschmid and Kunz report the history of a man, aged 56, whose occupation caused him to inhale trichlorethylene. He developed a severe retrobulbar neuritis with pupillary disturbances, paralysis of the hypoglossal nerve of the left side and polyneuritis of the nerves of all the extremities, with abolishment of the reflexes and reduction of the cutaneous sensitivity in the region of several peripheral nerves. The symptoms proved to be rather persistent and the vision seems to be permanently impaired. The authors call attention to the wide use of neurotoxic trichlorethylene, pointing out that it is employed as a fat solvent in industry as well as in cleaning fluids and other preparations that are marketed for home use.

Cause of Jaundice in Weil's Disease. — Kaneko states that studies carried out by his students disclosed that the direct diazo reaction in the serum develops promptly in Weil's disease. This and clinical observations led him to assume that the jaundice in this disease is connected with the passage into the blood of the bile which is in the bile duct system. The author's student Oka made the diazo test on fifteen patients with Weil's disease and on infected animals. The reaction was always diphasic; that is, the serum contained two types of bilirubin, the functional and the congestive types. Oka was able to show that the bile is discharged as the result of cell dissociation. The bile passage that results from cell dissocia-

tion shows the following aspects: Between the liver cells or the epithelia of the bile ducts there is a bile-colored mass, which exudes from the bile capillaries and from the lumens of the bile ducts, follows between the two cellular walls and is discharged into the yellowish perivascular edema. The author thinks that the bile-colored mass is bile. Oka observed that the only other condition in which this discharge of bile takes place is a jaundice that develops in dogs after poisoning with toluylene diamine. The author deduces from this that the jaundice in Weil's disease is likewise due to toxic action. He assumes that the toxin of the spirochetes first impairs and then dissolves the cellular cement substance. The result is cell dissociation and passage of the bile from the bile ducts into the lymph spaces and into the blood. Formerly the author assumed that the connection between the bile ducts and the blood was produced within the hepatic acini by the stasis of the pathologic bile in the impaired bile capillaries. However, Oka's studies disclosed that stasis is unnecessary and that the destruction of the cellular cement substance by the toxin of the spirochetes is the chief factor.

Policlinico, Rome

42: 1075-1122 (June 3) 1935. Practical Section

*Intolerance to Insulin: Case. D. Beggi.—p. 1075.
Intolerance to Intravenous Vaccine Treatment in Atypical Form of Undulant Fever: Case. E. Liverani.—p. 1082.
Gastric Resection Under Nupercaine Spinal Anesthesia: One Hundred Operations. R. Broglio.—p. 1088.

Intolerance to Insulin.—Beggi reports a case of diabetes in which the hypodermic injection of insulin (after the injections of insulin had been suspended for some time) was followed by the appearance of an urticarial reaction associated with edema of the face and neck. The intradermal reactions performed in the individual with various brands of insulin (Roche, Leo, Zanoni and Erba) all gave positive results. The reaction of insulin of the Serono brand produced the most marked positive reaction, manifested by the appearance of an area of erythema with a raised wheal at the site of the injection. The parenteral administration of deinsulinated pancreatic extracts (angioxil and astenil) did not produce any effects of intolerance in the patient. Experiments for the transfer of the patient's antibodies to rabbits gave the following results: The injection of a few drops of insulin of different brands in one of the ears of various rabbits, twenty-four hours after the injection of blood serum of the patient in the same ear, gave positive results with all brands of insulin, especially with that of the Serono brand. The injection of deinsulinated extracts in the other ear of each of the animals twenty-four hours after the injection of the blood serum of the patient in the same ear gave negative results in all cases. The intradermal injections of highly diluted insulin, but in increasing concentration, produced a temporary desensibilization in the patient, permitting him to continue his insulin treatment by the hypodermal route.

Prensa Médica Argentina, Buenos Aires

22: 1035-1082 (May 29) 1935. Partial Index

Choleriform Paratyphoid and Food Poisoning: Case. G. Elkeles and E. Barros.—p. 1044.
Intestinal Parasitism in Children. J. M. Pardina.—p. 1050.
*Cardiac Area in Rheumatic Fever in Children. J. C. Bertrand and J. R. Abdala.—p. 1063.

Enlargement of Cardiac Area in Rheumatic Fever.—Bertrand and Abdala say that the enlargement of the cardiac area, as determined by percussion, is a sign of value for the diagnosis of rheumatic fever in children, especially in cases of atypical forms of the disease in which the cardiac complications appear late in the disease or do not appear at all. The cardiac area enlarges more or less rapidly in all cases of rheumatic fever. In atypical cases the sign exists in the absence of the cardiac auscultatory symptoms and earlier than the appearance of changes in the electrocardiogram. The authors believe that the lack of tonus of the myocardium that results in the enlargement of the heart is due to the myocardial congestion and diapedesis originating from the impregnation of the myocardium by rheumatic toxins. Four atypical cases are reported. Two roentgenograms of the thorax of one of the patients, in whom murmurs did not exist, taken at a month's interval revealed the extraordinary change in size of the heart in so short an interval, showing the rapid modifications that the cardiac area may undergo in exceptional cases without murmurs.

Archiv für Kinderheilkunde, Stuttgart

105: 65-128 (May 31) 1935

Behavior of Allergy in Diphtheria. O. Chiari and J. Siegl.—p. 65.
*Reticulocytes in Lymphatism. Charlotte Hülsse.—p. 73.
Pathology of Bed Wetting. Z. von Gulácsy.—p. 81.
*Galactose Test in Children. B. Chomet. p.—86.
Atypical Diabetic Coma in Small Children. K. Hassmann.—p. 91.

Reticulocytes in Lymphatism.—Hülsse observed a relative increase in monocytes and lymphocytes in twenty-nine children with lymphatism, although the total number of leukocytes was normal in some of these children. In some cases a considerable increase in the reticulocytes was noted and interpreted as a symptom of an anemia that accompanies the lymphatism. This mild anemia in children with lymphatism is characterized by a comparatively slight decrease in hemoglobin and in the erythrocytes and by manifestations of brisk regeneration. On the other hand, reticulocytosis was absent in some children with severe lymphatism. Consequently the author considers it doubtful whether an increase in the reticulocytes can be considered as a criterion of the existence of lymphatism.

Galactose Test in Children.—Chomet reports the results of galactose tests on sixty children. He observed that the galactosuria was influenced by the body weight. In fifteen children the galactose test was made with the same quantity of galactose (40 Gm.) that is used in adults. However, since the values showed differences that corresponded to the various weight groups and since, moreover, the results obtained in the children with icterus were not entirely clear, the author made the galactose test with 30 Gm. on thirty-eight children without hepatic disorders. He found that the children who weighed more than 30 Kg. eliminated less than 2 Gm. of galactose, while the children who weighed less than 30 Kg. eliminated less than 3 Gm. Consequently the author assumed for children with a weight up to 16 Kg., in whom 30 Gm. of galactose had been administered, an approximate threshold value of galactosuria of 3 Gm. In adults, 3 Gm. is taken as the maximal normal value with an intake of 40 Gm. The author tested the galactose reaction also in a number of children with icterus. Nearly all these children showed values that noticeably exceeded the normal values and thereby indicated hepatic impairment. This became especially plain when, in children with icterus, the test was repeated every week. As the icterus subsided, a steplike reduction in the galactosuria could be observed.

Beiträge zur Klinik der Tuberkulose, Berlin

86: 211-288 (May 21) 1935

Studies on Two Strains of Acid-Fast Bacilli with Atypical Behavior from Cultures of Sputum of Tuberculous Patients. A. Mayer.—p. 213.
*Articular Rheumatism and Pulmonary Disorders. T. Rehberg.—p. 224.
Atelectasis or Infiltration? H. Starcke.—p. 236.
Pathogenesis of Solitary and Round Shadows in Roentgenogram of Lungs. J. Schemmel.—p. 248.
Indications for Collapse Therapy in Pulmonary Tuberculosis. B. M. Chmelnitzky.—p. 262.
*Quantitative Determination of Flocculation Capacity of Serum (Colloid Lability) in Tuberculosis. W. Molnár.—p. 284.

Articular Rheumatism and Pulmonary Disorders.—Rehberg thinks that infectious polyarthritis may be caused by tubercle bacilli as well as by numerous other pathogenic organisms. However, the incidence and the mechanism of the tuberculous origin have not been completely clarified as yet. Löwenstein's bacteriologic blood tests for the detection of tubercle bacilli have led some investigators to ascribe nearly all cases of polyarthritis to the tubercle bacillus, while others consider the tuberculous etiology of rheumatism extremely rare. The author describes several cases of pulmonary tuberculosis that concurred with polyarthritis. In one case the polyarthritis took a subacute course, the symptoms lasting about three months. The arthritic symptoms were refractory to salicylates, but they gradually disappeared following the subsidence of the glandular swellings. In another case the tuberculous articular rheumatism took a chronic course. The author calls attention to diagnostic difficulties, stressing that it is necessary to differ-

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entiate between caseous degenerative articular tuberculosis, tuberculous polyarthritis and ordinary infectious polyarthritis in a tuberculous organism. In discussing the factors on which the diagnosis of a tuberculous polyarthritis can be based, he expresses the opinion that the bacteriologic demonstration of tubercle bacilli in the blood (according to Löwenstein's method) is not yet suited to decide the diagnosis. The detection of tubercle bacilli in the articular punctate is of greater importance. The diagnostician must give his attention chiefly to the type of the primary tuberculous disorder and to the relation between the rheumatic symptoms and the beginning and further course of primary tuberculous disease. In the two aforementioned cases the parallelism was so noticeable that it was decisive for the diagnosis. However, when this parallelism is absent the diagnosis becomes doubtful. The author illustrates this in a case report. The absence of signs of new inflammatory or hematogenic processes made it doubtful that the articular disorder was of tuberculous origin, in spite of the fact that extensive tuberculous processes existed in the lungs. The assumption of an ordinary infectious polyarthritis was corroborated by the prompt action of salicylate. The author describes the history of a patient with bronchiectasis and with subchronic impairment of several joints in whom an acute articular rheumatism developed following an injection of histamine. He considers this articular rheumatism an allergic inflammation in an organism that had been sensitized by proteinic decomposition products developing in the bronchiectatic cavities.

Flocculation Capacity of Serum in Tuberculosis.—Molnár gives a review of the tests that have been suggested for the determination of the colloid lability in tuberculosis. These tests require large quantities of blood serum and they do not give entirely reliable results. The greatest disadvantage is that they are adapted to a certain point of the protein curve, so that only a single protein fraction can be determined with them. This disadvantage was eliminated by a quantitative micro-analytic method, which was developed by Darányi in 1931. The author found this method reliable but too complicated. He developed a simpler method and used Nissl's centrifugation tubes of 7 cc. capacity, which have a narrow lower portion of 0.5 cc. capacity with scale division. For the precipitation of the globulin fractions of the serum he found aluminum sulphate, in the 0.05 per cent solution as suggested by Mátéfy, most suitable. Like Mátéfy, he adjusted the test in such a manner that there develops no precipitate in healthy persons, whereas large amounts of precipitate appear in patients in whom tissue decomposition takes place. The author made this test approximately 2,000 times, chiefly on the serums of tuberculous patients. The reaction showed high values in thoracic empyema and in extensive cavernous tuberculosis of the exudative type. The highest values were obtained in carcinoma and in pleural and peritoneal exudates. In a number of cases the author observed that, if the reaction continued to show high values after pneumothorax treatment, exudates often developed later, whereas no exudate developed in cases in which the reaction disclosed improvement. High values were observed also in syphilis and in some instances in which clinical observation indicated only emphysema or diffuse bronchitis. In tuberculosis of the bones, higher values were obtained than were disclosed with other colloid reactions. Contrary to expectation, the values were low in catarrhal icterus, probably as the result of the presence of salts of the bile acids. If care is taken that centrifugation is continued for exactly two minutes at 1,500 revolutions, the reaction is well suited for comparative tests.

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Deutsche medizinische Wochenschrift, Leipzig

61: 901-940 (June 7) 1935. Partial Index

*Specific Allergens in Detection of Cause and in Treatment of Rheumatism and Gout. F. Gudzent.—p. 901.
Cavern Formation and Pulmonary Infarct. W. Hollmann.—p. 906.
Experiences with Meinicke's Serum Reaction for Tuberculosis in Children. J. Jochims.—p. 909.
Extensive Deposits of Lipoid Protein Crystals in Interstitial Substance of Kidney in Nephrosis with General Amyloidosis. E. Randerath.—p. 911.

Allergens in Rheumatism and Gout.—After Gudzent had observed a patient with gout, who had severe attacks every time he took milk treatment but who tolerated meat well, he studied a larger material and reached the conclusion that the acute attack of gout has no connection with acute deposits of uric acid but is rather an allergic reaction to a gout toxin. He observed also a number of patients with rheumatism, who stated spontaneously that they always felt worse after taking fish, eggs or milk. Skin tests with these substances resulted in wheal formation, and abstinence from these foods produced considerable improvement. Further studies on this problem led him to the following conclusion: Rheumatic processes in the joints, muscles, nerves, tendons and blood vessels are the manifestation of a hyperergic reaction resulting from a hereditary or acquired hypersensitivity to a foreign protein. This protein may come from food, fermented drinks, pathogenic or nonpathogenic micro-organisms, mold fungi, yeast fungi or other substances. He made tests with various types of protein on 300 patients with rheumatic disorders and obtained positive reactions in 279 cases, 34 per cent showing a positive reaction to cereal proteins, 29.7 per cent to meat or fish proteins, 16.7 per cent to vegetable proteins, 9 per cent to bacterial proteins, 7.6 per cent to proteins from milk or eggs and 2 per cent to mold or yeast fungi. In patients in whom the test disclosed a sensitivity for a food protein, the author tried to eliminate the offensive substance from the diet, and a change of residence was prescribed for patients with a hypersensitivity to mold fungi. He admits that rheumatism and gout, after they have once developed, may be prolonged by secondary factors, such as cold, dampness, trauma, change in the weather and psychic factors, even if the primary cause has been eliminated. For this reason he attempted desensitization by means of intragluteal injection of the offensive allergen. At first the injections were given two or three times each week, then twice and finally only once a week. The entire treatment required from six to twelve weeks and more. He observed that the size of the dose does not determine the curative effect, and he commenced with small doses gradually increased to 1 and 2 cc. in order to avoid severe reactions. Because the condition was rather severe in the patients in whom this treatment was employed, he did not expect complete recovery but hoped to counteract the pains and swellings and to reestablish at least partly the working capacity. He was able to realize these aims in a satisfactory manner.

Klinische Wochenschrift, Berlin

14: 769-808 (June 1) 1935. Partial Index

Studies on Vitamin B_2. W. V. Drigalski.—p. 773.
*Iodometric Studies on Normal and Pathologic Human Urine. W. Ruziczka.—p. 775.
Menstruation Produced by Artificial Corpus Luteum Hormone. C. Kaufmann.—p. 778.
*Cholesterol Content and Cholesterolytic Capacity of Serum in Vitro in Skin Diseases. H. Hruszek.—p. 779.
Concurrence of Acute Miliary Tuberculosis and Panmyelophthisis? H. Kreich and F. Heni.—p. 781.
Blood Fat Reactions in Endogenic Emaciation. G. Borruso.—p. 783.

Iodometric Studies on Human Urine.—Ruziczka shows that, in analyzing human urine with the rapid method of determination of the iodine number according to Margosches, Hinner and Friedmann, the values obtained are higher (iodine number I) than in case of direct titration with solution of iodine in potassium iodide, as prescribed by Lieb and Lanyar for the determination of homogentisic acid (iodine number II). Uric acid shows, in a 0.1 per cent solution, under conditions that obtain in the rapid method, even a higher iodine number than that which corresponds to the adding on of a molecule of hypoiodous acid. Accordingly, the carbonyl groups of the uric acid molecule do not act sterically to inhibit the saturation of the double linking. Thus the iodine number expresses also the uric acid content of the urine. If the iodometric acid determination according to the modification of Kolthoff is used, the urine always shows lower values than is the case in acidimetric titration and there is in this case no uniform relationship to the hydrogen ion concentration. These lower values are chiefly the result of the fact that an iodine consumption takes place under these conditions. That this is so is proved by the fact that, by the addition of the iodometric acidity and the iodine number II, a value is obtained that approximately tallies with the acidimetrically determined acidity. There is no regular proportionality between the "iodometric acid number" and the

"saponification number." To be sure, in many cases, such as in the urine of patients with diabetes mellitus, the terminal point in titration with hydrochloric acid is hardly detectable.

Cholesterol Content of Serum in Skin Diseases.—Hruszek describes experiments conducted to determine whether the serum of healthy persons and of persons with skin diseases, particularly psoriasis, has the capacity to dissolve cholesterol in vitro. The same tests were made also on the serums of persons who had been subjected to a cholesterol tolerance test. The author observed that some serums dissolve a portion of the cholesterol that has been added in vitro; these serums show positive lysis values. Other serums do not change their cholesterol content following the lysis experiment; their lysis value is zero. A third group of serums shows, following the completion of the in vitro test, lower values than before, which makes the lysis value of these serums negative. These three types of serums are found in normal persons as well as in those with skin diseases, so that the cholesterolytic capacity is no indicator of the one or the other skin disease. Patients with psoriasis may have any of the three types of serum, whether they have been subjected to a cholesterol test or not. The author concludes from this that the cholesterol values of the serum are no indicators of the existence of a lipoidosis in psoriasis as was suggested by Grütz and Bürger. He thinks that the pathogenesis of psoriasis is still unsolved.

Münchener medizinische Wochenschrift, Munich

82: 857-898 (May 30) 1935

Ozone Therapy in Surgery. E. Payr.—p. 857.
*Matti's Procedure of Spongiosa Implantation in Bone Fractures and Pseudarthrosis. F. König.—p. 860.
Treatment of Bone Fractures That Heal Slowly or Not at All. W. König.—p. 862.
*Hepatic Function and Suitability for Surgical Treatment. W. König. —p. 863.
Clinical Aspects and Therapy of Chronic Digestive Weakness During Childhood (Heubner-Herter's Disease). E. Holzmann—p. 864.

Spongiosa Implantation in Fractures and Pseudarthroses.—König says that Matti in 1929 suggested that in a pseudarthrotic tibia the medullary cavity be opened at the site of fracture, after the periosteum has been pushed aside; then the connective tissue that has formed between the fractured ends is removed except at the posterior wall, where the fibrous connection is preserved. Then the femur is opened, through a longitudinal incision, below the greater trochanter by a periosteum-bone flap down to the spongiosa. Material from the spongiosa is withdrawn and is introduced like mortar into the tibial cavity and between the freshened ends of the pseudarthrosis. The periosteum is closed and the skin sutured. The bone cover is replaced on the femur and the skin is closed. König employed this procedure in four cases. In one of these cases a local infection set in and the method failed, but in the three others the procedure was successful. The author describes these three cases and reaches the conclusion that Matti's transplantation of the spongiosa is a simple method that can be employed with good success in bone fractures of the diaphysis that do not heal, as well as in pseudarthrosis.

Hepatic Function and Surgical Treatment.—König believes that in surgical operations failures are often the result of impairments of the liver that were not recognized before the operation. The significance of this problem goes beyond the scope of the surgical interventions on the liver or the biliary tract, for the function of the liver becomes impaired as the result of the anesthesia, the operation and the fasting period that usually follows. He deplores that most of the functional tests of the liver are too complicated for the surgeon and stresses the necessity of simple tests. He concedes that the urobilin and urobilinogen tests are helpful but considers them insufficient. He accepts Mancke's suggestion, according to which Millon's test of the urine is helpful in estimating the hepatic function. His own experiences with Millon's test convinced him that patients in whom the test is positive before the operation are in danger. If such patients absolutely require an operation, attempts should be made to improve the hepatic function before the intervention by medication with insulin and dextrose.

Wiener klinische Wochenschrift, Vienna

48: 791-814 (June 7) 1935. Partial Index

*Compression Treatment of Phlebitis. E. Friedländer.—p. 791.
*Part Played by Pleximeter and by Thoracic Wall in Mechanism of Percussion. A. Winkler.—p. 794.
Shortening and Lengthening of Nose. E. Eitner.—p. 799.
Sign of Lesion of Pyramidal Tract in Upper Extremity. R. Rosner. —p. 800.

48: 815-838 (June 14) 1934. Partial Index

Addiction to Narcotic Poisons and Breaking of Drug Habit, Particularly with Regard to Morphine. C. Amsler.—p. 815.
*Compression Treatment of Phlebitis. E. Friedländer.—p. 818.
Newer Method of Iontophoresis. Martha Brünner-Ornstein.—p. 822.
Encephalitis During Childhood. J. Zappert.—p. 824.
Intracranial Lesions Sustained During Birth. H. Heidler.—p. 825.

Compression Treatment of Phlebitis.—According to Friedländer, thrombus formation in the venous circulation is one of the most difficult problems in medicine. He points out that it was Fischer who first advised that inflammations in thrombophlebitis be counteracted by compression and that the danger of embolism be averted by exercising the inflamed extremity. Fischer's mode of treatment made it possible for the patients to get up and follow their occupation as soon as the compression bandage had been properly applied with a paste consisting of zinc oxide, gelatin, glycerin and water. It is the aim of the compression bandage to reestablish the disordered circulation, to counterbalance the internal inflammatory pressure by pressure from the outside and to force the thrombus in its entire length against the venous wall. The author emphasizes that the pressure must be carefully adjusted to the individual needs, and he describes various ways of applying the compression bandage. He calls attention to the difficulties encountered in the diagnosis of a thrombophlebitis. He concedes that in the subcutaneous vessels the condition is usually readily recognized, but even in such cases erroneous diagnoses are possible. Rheumatic pains in muscles and sciatica may lead to diagnostic mistakes in the deeper thromboses. A thorough internal examination is of vital importance. The condition of the heart must be known in order to regulate the circulation properly. Urinalysis may disclose cystitis, cystopyelitis or diabetes mellitus. The latter condition particularly may influence the course of thrombophlebitis. A former syphilitic infection and the average alcohol consumption may be important, as may also foci of infection. The condition of the lungs should be known, and the family anamnesis should give attention to such conditions as varicose veins, leg ulcers and phlebitis. The author advises that the compression treatment be instituted as early as possible. The duration of the treatment differs. As a rule it requires from four to eight weeks, but the patient may follow his occupation during this time. The patient should not use crutches or other supports. The author employed the compression bandage in 196 cases and observed only one fatal embolism, in a woman with pelvic thrombosis. He did not observe a single fatality among the patients with thrombosis of the leg or thigh who were subjected to compression treatment.

Pleximeter in Mechanism of Percussion.—Winkler analyzes the factors involved in percussion and shows the shortcomings of the hitherto accepted theories about the part played by the pleximeter and by the thoracic wall. The efficacy of percussion as a comparative and demarcating method of examination is determined by the diameter that goes through the entire depth of the normal lung. The optimum of percussion is obtained when weak blows with light elastic hammers hit lightly applied, stationary, small-surface, readily flexible pleximeters or unilaterally movable, large-surface, elastic pleximeters. The percussion sound of the lung is a sound mixture, in which the tissue sound of the axial penetration zone is the less masked by the other sound components, the more the axial mechanical blow effect approaches the optimal. Every change in the percussion capacity of the pulmonary tissues within the axial penetration zone influences the character of the sound. The pleximeter makes possible a uniformity of factors by obviating differences in the time, surface and power of the blows and thus is a great aid in the practical utilization of percussion as a demarcating and comparative method of examination.

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Zeitschrift für klinische Medizin, Berlin

128: 121-222 (May 24) 1935. Partial Index

*Studies on Galactose Assimilation in Patients with Diabetes Mellitus. C. A. A. Schrumpf.—p. 121.

Myocardiac Infarct: Symptomatologic and Diagnostic Survey of Twenty-Eight Cases. J. E. Holst.—p. 130.

*Biliary Pigment in Blood in Case of Cardiac Decompensation. J. B. Milovanović and L. Stanojević.—p. 163.

Behavior of Basal Metabolism and of Iodine Content of Blood in Thyrotoxicoses. W. Möbius and F. A. Nolte.—p. 174.

Relations Between Internal and External Secretion of Pancreas: Herxheimer-Mansfield Phenomenon in Pancreolithiasis. E. Friedlander.—p. 184.

Galactose Assimilation in Patients with Diabetes Mellitus.—Schrumpf observed, following galactose tolerance tests (40 Gm. of galactose) on eleven patients with diabetes mellitus, that the blood sugar content is higher. This increase is observable after one hour in the cutaneous as well as in the venous blood. The residual reduction in the blood shows after one hour a moderate increase, which is an indication of a rise in the galactose content. This gain is noticeable in the cutaneous as well as in venous blood; however, in respect to quantity it is less than the total increase in the blood sugar. It appears that the galactose, which is demonstrable in the blood of patients with diabetes mellitus, is not retained in the peripheral tissues. The urine contained galactose in only three out of eleven patients, and the quantities were so small that in view of the ordinary clinical evaluation of tolerance tests they cannot be considered pathologic. The galactose tolerance test was followed by noticeable glycosuria in only two patients, and in these the diet had not had the proper caloric composition. It appears that patients with diabetes mellitus can assimilate small amounts of galactose. The author thinks that the results he obtained in these studies indicate that galactose can be used more extensively in diabetes mellitus.

Biliary Pigment in Blood in Cardiac Decompensation.—Milovanović and Stanojević call attention to the fact that cardiac decompensation influences the hepatic function. In severe cardiac decompensation there often exists a slight jaundice, and many investigators agree that jaundice indicates an unfavorable prognosis in patients with cardiac decompensation. The publication of methods for the determination of biliary pigment in the blood has revived interest in the question of bilirubinemia in patients with heart disease, for these methods make it possible to detect a latent jaundice. The author reviews the literature on bilirubinemia in heart disease and then describes his own studies. He emphasizes that it is necessary to determine the bilirubin content of the serum and the function of the cardiovascular apparatus simultaneously. He determined the hydrodynamic condition of the cardiovascular system by means of the constant of Pachon and Fabre and the biliary pigments by the method of Hijmans van den Bergh. He reaches the conclusion that the prognosis is unfavorable in cases in which the constant is low, as well as in cases in which the constant decreases while the bilirubinemia rises.

Zentralblatt für Gynäkologie, Leipzig

59: 1329-1392 (June 8) 1935

*Elimination of Thyrotropic Substance in Urine of Menopausal Women. P. Grumbrecht.—p. 1331.

Clinical Observations on Growth of Uterus Effected by Estrogenic Substance. M. Ito and C. Nagai.—p. 1336.

Large Varix of Vein of Umbilical Cord. H. Dworzak.—p. 1340.

Delivery in Dorso-Anterior Frontal Presentation. K. Nordmeyer.—p. 1343.

Behavior During Operation in Unrecognizable Cause of Intra-Abdominal Hemorrhage. E. Redenz.—p. 1347.

Pubiotomy: Case. A. Niedermeyer.—p. 1352.

Elimination of Thyrotropic Substance in Urine of Menopausal Women.—Grumbrecht points out that the anterior lobe of the hypophysis excretes, in addition to the growth and sex hormones, a substance that stimulates the thyroid to greater activity. Whereas the mode of action of the thyrotropic hormone is well known, its mode of elimination is not so well understood as yet. Accordingly, the author decided to test the urine of menopausal women for the presence of the substance, because the symptoms that appear in menopausal women (rushing of blood to the head, sweating and palpitation of the heart) are all symptoms indicating increased thyroid activity. An extract was prepared from the urine of these women and was injected into infantile rabbits, which promptly developed accelerated heart action and other symptoms. Some of the animals died; the others were killed on the third day. The thyroids of the animals were subjected to histologic examination, which revealed changes indicating increased functional activity. The urine of the women who were in the early or late stages of the menopause produced less severe changes. The urine eliminated during the menstrual period likewise seemed to contain thyrotropic substance, while the urine of sexually mature women outside the menstrual period did not produce changes in the thyroid of the animals. The author concludes from these observations that the menopausal disturbances are the result of overfunctioning of the anterior lobe of the hypophysis, which is induced by the abolishment of the gonadal function. The treatment should attempt to reduce the thyrotropic action. This can be accomplished by the administration of iodine or of estrogenic substance. The author recommends di-iodotyrosin (3.5 di-iodo-4-oxyphenylalanine) either alone or in combination with the estrogenic preparations for the treatment of menopausal disorders.

Ortopediya i Travmatologiya, Kharkov

6: 1-126 1934. Partial Index

Torsion Spasm and Orthopedic Corset. N. A. Zolotova.—p. 7.

*Histologic Study of Parathyroids in Chronic Rheumatic Polyarthritis and Spondylo-Arthritis. B. I. Shkurov and K. F. Elenevskiy.—p. 17.

Ankylosing Polyarthritis. E. Ya. Kalikhman.—p. 28.

Tuberculous Spondylitis. F. O. Berkhina, M. A. Pogorelskiy and A. P. Kotov.—p. 33.

*Late Results of Tendon Transplantation for Flaccid Paralysis of Lower Extremities. B. V. Rubinshtein.—p. 67.

Parathyroids in Chronic Rheumatic Polyarthritis.—Shkurov and Elenevskiy examined ninety-one histologic preparations of parathyroid tissue removed for therapeutic purposes from seventy-seven patients, thirty of whom were suffering from chronic rheumatic polyarthritis and forty-seven from spondylo-arthritis. The presence of parathyroid tissue in the removed material was established in each instance by histologic examination. The size of the glands removed did not exceed that given by most authors for the normal gland. On the basis of their observations the authors suggest that the secretory reaction is in all probability not limited to the chief cells and that the oxyphil cells likewise have a secretory function. They found oxyphil cells singly and in islets in fifty-three preparations, cells representing a transitional stage from the chief to the oxyphil type in thirty-four and a colloid-like substance in thirty-two. Clinically the cases presented increased blood calcium content, stiffness and ankylosis of the joints. The preoperative blood calcium was above normal in twenty-two (up to 16 mg.), normal in eleven and below normal in only two. The twenty-two patients with hypercalcemia showed, after parathyroidectomy, an average diminution of 3 mg. per hundred cubic centimeters of blood serum. The clinical results were gratifying. Of the eighty-one patients submitted to partial parathyroidectomy, only three did not show any improvement, and in two the progress of the morbid condition was not arrested. The authors conclude that the oxyphil cells signify an increased function of the parathyroid and that chronic rheumatic polyarthritis and spondylo-arthritis are caused by hyperactivity of the parathyroid glands.

Results of Tendon Transplantation for Flaccid Paralysis.—Rubinshtein reports the late results of tendon transplantation for flaccid paralysis of the lower extremities performed by Vreden in the Central Traumatologic Institute. The duration of observation was from one to twenty-one years. The patients were operated on from one and one-half to twenty-five years after the onset of paralysis. In their experience, good results could not be expected if patients were operated on earlier than three years after the onset of the paralysis. The controversial points among orthopedic surgeons with regard to operative indications center about the age of the patient and the duration of the paralytic state. The author feels that the most important element in the success of the operation is the correct evaluation of the strength and synergistic capacity of the muscle to be used as a substitute. He found Hübscher's table of relative strengths of the nine main muscles of the foot fairly reliable. While preservation of the sheath of the tendon is of great theoretical importance for the survival of the trans-

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planted tendon, it was not done once in their work because of technical difficulties. Of the 238 operations performed on 215 patients, good results were noted after 220, satisfactory after twelve and poor after six. Advantages of tendon implantation under an osteoperiosteal bridge are emphasized.

Nederlandsch Tijdschrift voor Geneeskunde, Haarlem

79: 2887-3002 (June 15) 1935

Hydronephrosis. J. A. Weijtlandt.—p. 2888.
*Positive Venous Pulse. P. Formijne.—p. 2895.
Lung Collapse in Children. M. De Bruin.—p. 2902.
House Physician and His Contribution to Medical Science. E. D. Wiersma.—p. 2915.
Vitamin D Content of Cod Liver Oil. L. W. Van Esveld.—p. 2924.
*Simple and Sensitive Test for Bilirubin in Urine. A. W. J. H. Hoitink.—p. 2928.

Positive Venous Pulse.—Formijne studied the venous pulse of four patients in whom there was simultaneous contraction of the auricle and the ventricle. One patient showed a strongly positive venous pulse due to marked delay in the conduction time. Another had a 2:1 auriculoventricular block. The blocked P wave occurred simultaneously with the contraction of the ventricle. The venous pulse was weakly positive. A third patient showed nodal rhythm and a positive venous pulse. The last patient had a history of nodal rhythm with a negative venous pulse. One year later she developed an arrhythmia in which the P wave occurred at the same time as the ventricular contraction. A synchronism of the auricular and ventricular systole resulted. These cases indicate (1) that a positive venous pulse may appear if the auricular contraction through some mechanism accompanies the ventricular systole, but that (2) the intensity of the positive venous pulse may vary greatly or may be absent. In order to explain these differences the author investigated the expansion and contraction of the right auricle, of the junction of the vena cava superior and the right auricle, and of the large vessels. A varying degree of competence of the valvular mechanism at the junction of the vena cava superior and the right auricle is advanced as a possible explanation of the positive reaction. The contractile power of the auricle may play a part in the causation or failure of the venous pulse. To illustrate the importance of the condition of the large veins the author presents a patient in whom a unilateral left positive venous pulse was found, which he ascribed to a tricuspid incompetence associated with the presence of a left vena cava superior.

Test for Bilirubin in Urine.—Hoitink experimented with a modification of Fouchet's test for bilirubin in the urine. The following technic was used: About 10 cc. of urine is put in a test tube. If the reaction is not weakly acid, it is made so by means of acetic or hydrochloric acid. Half the volume of the urine (5 cc.) of a 10 per cent solution of barium chloride is added. The contents of the tube are mixed well and filtered. The filter paper with the precipitate is spread on a ground glass slide or on another piece of white filter paper. One drop of Fouchet's reagent is applied to three different places on the border of the precipitate. After five minutes a blue or greenish color indicates bilirubin. The author detected 0.05 mg. of bilirubin per liter of urine. He found the test more sensitive and simpler than the Gmelin, Huppert-Salkowski-Steensma and other tests.

Norsk Magasin for Lægevidenskapen, Oslo

96: 449-560 (May) 1935

*Tuberculosis of Heart and Tuberculous Changes in Great Arteries. E. Dahl.—p. 449.
Investigations on Iron Metabolism in Pregnancy: IV. Iron Store of the New-Born Infant. K. U. Toverud.—p. 468.
Three Rare Urologic Cases. C. Johannessen.—p. 482.
Coxa Vara Infantum: Case. C. Johannessen.—p. 493.
Ruptured Mesenterial Chyle Cyst: Two Cases. L. E. Volodarsky.—p. 496.

Tuberculosis of Heart and Great Arteries.—Dahl reviews the subject, citing cases, and reports three instances. While the cases of chronic tuberculous changes found by him in the literature were localized particularly in the aorta, in his patient, a girl aged 10 years, presenting acute miliary tuberculosis, there was an infiltration 2 cm. long, 4 mm. wide at the widest point and extending 3 mm. into the lumen, in the left pulmonary artery. Microscopic examination disclosed a true conglomerate tubercle, entirely localized in the intima. From the size and the marked cheesy necrosis of the infiltrate, in contrast to the apparently recent miliary tubercles in the various organs, and from the beginning invasion of the media, he regards this as an older process, originated by direct infection through the blood stream and as the starting point of the miliary tuberculosis. The primary focus was not discovered. In the second patient, a woman aged 29, the hematogenous metastases could be localized in the valves of the heart. A tubercle, larger than the head of a pin, was found in the anterior mitral valve. The infiltration, situated under the elastic membrane of the valve endocardium, presented a marked cheesy necrosis, surrounded by typical granulation tissue with giant cells, and had invaded the adjacent valve endocardium. Abundant tubercle bacilli were found. In the third patient, a man aged 70, with cancer of the stomach and no signs of heart disorder or circulatory disturbance, the apex of the left lung was the seat of two inveterate, partly calcified infiltrations the size of a pea. On the wall of the left ventricle was a round, well defined tumor the size of half a walnut, firm and smooth, and in the ventricle, corresponding to the tumor, was a layer of thrombus masses. Microscopically the tumor consisted of a homogeneous, structureless mass surrounded by granulation tissue without special characteristics, continuing directly into the thrombus stratum. Tubercle bacilli were present in great numbers. The process is assumed to have originated by hematogenous infection from the older lung disturbance in the left apex. The heart was of usual size, without hypertrophy of the musculature of the left ventricle.

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*Investigations on Blood Sugar and Liver Function in Various Skin Diseases. G. Guldberg and L. Hannisdal.—p. 561.
*Acute Myocarditis in Nonseptic Gonorrhea. G. Guldberg.—p. 576.
Erysipeloid. R. Strøm.—p. 581.
Frequency and Localization of Arthritis Deformans Among Lapps. K. E. Schreiner.—p. 592.
Tuberculosis Mortality and Tuberculosis Morbidity. K. F. Andvord.—p. 599.

Blood Sugar and Liver Function in Skin Diseases.—Guldberg and Hannisdal's material comprises sixty-four cases in which five of the patients (two with exfoliative dermatitis, two with chronic eczema and one with mercury dermatitis), in addition to low fasting blood sugar, had marked posthyperglycemic hypoglycemia, the values falling as low as 29 mg. per hundred cubic centimeters without certain signs of hypoglycemic reaction. In four of the patients, treatment with dextrose injected intravenously together with insulin was promptly effective.

Acute Myocarditis in Nonseptic Gonorrhea.—Guldberg's case shows that, in a person with gonorrheal urethritis and prostatitis with afebrile and wholly favorable course and without clinical or bacteriologic signs of general infection, grave cardiac complications may occur in the form of acute myocarditis, which in this instance set in after three weeks. The electrocardiogram revealed a partial atrioventricular block and did not become normal until four months had passed.

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*Dyspeptics: Contribution to Pathology of Some Chronic Gastro-Intestinal Disorders Especially on Basis of Clinical Observations on Functional Relations in Vegetative System in One Hundred Patients Having Digestive Disorders. M. S. Kobro.—p. 1.

Pathology of Chronic Gastro-Intestinal Disorders.—Kobro's cases, all in adults, represent chronic unspecific disorders of the digestive tract without complicating disturbances. No definite physical type, he says, is characteristic of patients with dyspepsia, although 50 per cent of the patients were leptosomatic. Extensive indications of a vegetative neurosis were seen in all cases, apparently with a vagotonic predominance. He concludes that there is a close relationship in all digestive disorders and between these and the vegetative neurosis, which he assumes to be primary. Chronic dyspepsia is a forerunner of gastric ulcer. The vegetative neurosis is the expression of a toxic condition of the organs. The unknown toxin acts in two ways, producing a vegetative lability and a toxic gastritis; these together cause the erosions and thus the ulcer. Constipation, colitis, so-called primary chronic appendicitis, different phases of chronic dyspepsia, gastritis and peptic ulcers are different stages and different anatomic localizations of one and the same pathologic condition.